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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

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MANUFACTURE, PACKING, STORAGE AND INSTALLATION OF MEDICAL DEVICES

Regulations Establishing Good Manufacturing Practices

[4110-03]

Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

[Docket No. 75N-0140]

PART 809—IN VITRO DIAGNOSTIC PRODUCTS FOR HUMAN USE

PART 820—GOOD MANUFACTURING PRACTICE FOR MEDICAL DEVICES: GENERAL

Regulations Establishing Good Manufacturing Practices for the Manufacture, Packing, Storage, and Installation of Medical Devices

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document establishes a good manufacturing practice (GMP) regulation for the manufacture, packing, storage, and installation of medical devices. This regulation implements a provision of the Medical Device Amendments of 1976.

EFFECTIVE DATE: December 18, 1978.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: On May 28, 1976, the Medical Device Amendments of 1976 (Pub. L. 94-295) were enacted into law, amending the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 201 et seq.). Section 520(f) of the act (21 U.S.C. 360j(f)) provides the agency with authority to prescribe a regulation requiring that the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of medical devices conform to current GMP requirements, as prescribed in the regulation, to assure that devices are safe and effective and otherwise in compliance with the act.

The proposed device GMP regulation was published in the FEDERAL REGISTER of March 1, 1977 (42 FR 11997). Other FEDERAL REGISTER notices concerning this regulation are cited below in the section of this preamble on "History of Device GMP Regulation."

The Commissioner recognizes that the medical device industry consists of manufacturers whose devices and manufacturing processes differ significantly. This diversity of manufacturing processes affects the development of comprehensive GMP regulations that will apply to all finished device manufacturers. The Commissioner believes that an "umbrella" GMP regulation applicable to all finished device manufacturers should not be so specific as to prescribe for each manufacturer the precise details of what it must do and how it must undertake to manufacture devices. Rather, the GMP regulation should contain general requirements in specific areas of concern applicable to all manufacturers, specify additional requirements for certain devices, and require each manufacturer to supply the details which are appropriate for its device by developing for the manufacture of each device a detailed set of procedures which implement the GMP regulation. FDA will examine such procedures to determine whether a manufacturer is complying with the regulation.

The Food and Drug Administration (FDA) expects to publish additional GMP regulations applicable to specific types of devices. These future regulations will supplement the "umbrella" GMP regulation and will be of two types: One will contain requirements that will apply only to generic types of devices or classes of devices, e.g., pacemakers, eyeglasses, etc.; the other will contain requirements that will apply to certain devices or cross-class characteristics or processes, e.g., sterile devices, plastics, electrical properties, etc.

The "umbrella" GMP regulation imposes additional requirements on "critical devices," defined as devices that are intended for surgical implant into the body or devices intended to support or sustain life and whose failure to perform when properly used can be reasonably expected to result in significant injury to the user. Other devices are called "noncritical" devices and are subject to provisions of the regulation that are not limited to critical devices. The distinction is based on the additional risks to users that are posed by defective critical devices.

This distinction was incorporated into the proposed regulation published in the FEDERAL REGISTER of March 1, 1977 (42 FR 11997), by means of a two-tier approach that denotes general requirements applicable to all devices (critical and noncritical) and specific requirements applicable only to those devices classified as "critical."

IMPORTANCE OF DEVICE GOOD MANUFACTURING PRACTICE REGULATION

Today, increasing numbers of Americans are experiencing the benefits of modern medical technology in the treatment of injury and disease. Device manufacturers, adapting advances in space and medical technology, are producing a broad spectrum of varied and complex life-sustaining, life-supporting devices. In addition, a growing number of other, less sophisticated devices also have been made available to health professionals for improved health care services delivery. At the same time, Americans are also more likely to come in contact with devices. Data compiled by the American Hospital Association show that, during 1976, there were more hospital admissions, outpatient visits, and physician visits in the United States than in any preceding year (Ref. 1). As a consequence, more devices than ever before were used by and on Americans in the diagnosis and treatment of medical conditions.

Consumers who use devices differ from other consumers in an important respect. They are usually injured or diseased, and thus are a population at risk. These patients, and the many health professionals who diagnose and treat their conditions, depend on and trust device manufacturers to produce safe and effective devices of high quality. Although the degree of a patient's dependence on a device varies according to the nature of the illness, it is clear that the application of defective devices to patients already at risk because of illness could have a deleterious or even catastrophic effect on their recovery.

Based on FDA's experience, the Commissioner believes that it is vitally important that devices be manufactured in accordance with quality assurance principles that help prevent the production of defective products that can endanger consumers. In monitoring device recalls, FDA has found that, too often, device manufacturers have fallen short in meeting the expectations of those who need and depend upon high quality medical products. During the past several years, FDA monitored approximately 1,000 device recalls. Many of these resulted from manufacturers' failure to follow good manufacturing practices. For example, of 232 device recalls monitored by the FDA from October 1976 through November 1977, FDA believes that 198 of them were attributable to poor manufacturing practices.

The quality assurance program mandated by this regulation is designed to be preventive. The device GMP regulation requires all device manufacturers to design, implement, and continually monitor a comprehensive quality assurance program. This quality assurance program may be appropriately tailored to satisfy a device's special manufacturing requirements, but it may not compromise strict quality

control standards. Based on its experience, FDA believes that manufacturers who operate in accordance with the requirements of the regulation will be less likely to distribute defective devices to an unwary public than those who do not meet the requirements. Quality assurance under this regulation will maximize the probability that only safe and effective devices will reach the marketplace.

The device GMP regulation has been developed in accordance with basic principles of quality assurance. (See, for example, Juran, "Quality Control Handbook," 3d ed., McGraw-Hill (1974).) These principles have as their goal the production of articles that are fit for their intended uses, and may be stated as follows: (1) Quality, safety, and effectiveness must be designed and built into the product; (2) quality cannot be inspected or tested into the finished product; and (3) each step of the manufacturing process must be controlled to maximize the probability that the finished product meets all quality and design specifications.

During 1977, FDA conducted approximately 300 device establishment inspections to survey current manufacturing practices (Ref. 2). This survey showed that the majority of device manufacturers already had quality assurance programs in place that complied with about half of the provisions of the proposed device GMP regulation. This survey also shows, however, that many firms are not adhering to procedures that fulfill basic principles of quality assurance. As firms comply with the requirements of the regulation, FDA expects that many device defects and recalls can be avoided. The Commissioner believes that promulgation of a device GMP regulation will help prevent defective devices from reaching the marketplace and will help assure the production of safe and effective devices.

History of Device GMP Regulation

Since December 1973, FDA has been actively involved in the development of a GMP regulation for medical devices. Representatives of the general public and industry were invited and encouraged to assist the agency in this effort.

During the summer of 1975, a preliminary draft of a device GMP regulation was developed by the agency. Because of the widespread interest in this subject, the Commissioner made this draft regulation available to the public for comment and review before a proposed regulation was published in the Federal Register. A notice of availability of the draft regulation was published in the Federal Register of August 8, 1975 (40 FR 33482). Interested persons were given 60 days to submit comments. In view of the interest generated by the draft regulation and after a review of the initial comments, FDA decided to hold public meetings on the draft regulation in four major cities. These meetings were announced in the Federal Register of October 9, 1975 (40 FR 47530). The four public meetings were held in November 1975 in Dallas, San Francisco, Chicago, and Washington, D.C. Approximately 1,200 persons attended these four meetings, and all questions and comments were recorded and transcribed (ref. 3).

In addition to reviewing the comments received at the meetings, FDA reviewed approximately 130 written comments on the draft regulation. Based on these comments, FDA developed a proposed GMP regulation, which was published in the Federal Register of March 1, 1977 (42 FR 11997). Interested persons were given until June 29, 1977 to submit comments and views on the proposal. Drafts of the final regulation were made available to the public by notices published in the Federal Register of October 25, 1977 (42 FR 56348) and March 7, 1978 (43 FR 9320).

Device GMP Advisory Committee

Section 520(f)(3) of the Federal Food, Drug, and Cosmetic Act requires that the Commissioner of Food and Drugs establish an advisory committee for the purpose of making recommendations to him on the proposed regulation and the approval or disapproval of petitions requesting exemptions or variances from GMP requirements that may be submitted to FDA by manufacturers and referred to the committee by FDA.

This advisory committee, known as the Device GMP Advisory Committee, is composed of nine members. Three of the members represent Federal, State or local government; two members represent the interests of physicians and other health care professionals; two members represent the interests of the device manufacturing industry; and two members represent the interests of the general public.

A notice requesting nominations for members of the Device GMP Advisory Committee was published in the Federal Register of July 13, 1976 (41 FR 28817); a notice announcing the establishment of the committee was published in the Federal Register of August 27, 1976 (41 FR 36233).

A notice in the Federal Register of June 28, 1977 (42 FR 32805) announced that the Device GMP Advisory Committee would hold its first meeting on August 4, 1977 and that a public hearing to hear views on the proposed GMP regulation would be held on August 5, 1977.

During the first advisory committee meeting, representatives of FDA's Bureau of Medical Devices reviewed the events which led to the development of the proposed regulation, discussed the agency's philosophy on good manufacturing practices, and presented a summary of the comments received on the proposal (Ref. 4). The advisory committee reviewed these comments and provided its own general and specific comments to the agency.

At the August 5, 1977 public hearing, the Director of FDA's Bureau of Medical Devices served as the presiding officer and was assisted by a hearing panel, which included the Device GMP Advisory Committee and representatives from the Bureau and regional offices. Representatives of five trade associations, one manufacturer, FDA, and the general public presented comments and suggestions. This hearing was attended by approximately 200 persons, and transcripts of the meeting and hearing are available (Ref. 5).

During the Advisory Committee meeting and public hearing, the following six major issues relating to a GMP regulation were identified as warranting further discussion:

1. Effective date of the regulation.
2. Exemption or variance procedure.
3. Applicability to foreign manufacturers.
4. Disclosure of internal audits.
5. Inflationary impact.
6. Definition of a "critical device."

The advisory committee agreed to consider each of these issues in detail at its next meeting. The agency asked for additional written comments from the advisory committee and agreed to prepare a draft final rule, also to be discussed at the next meeting, reflecting the changes made as a result of the agency's review of written comments, public testimony, and committee recommendations.

A notice was published in the Federal Register of September 13, 1977 (42 FR 45960) announcing that the second Device GMP Advisory Committee meeting would be held on October 27-28, 1977. A notice of availability of the draft final regulation was published in the Federal Register of October 25, 1977 (42 FR 56348). At the meeting, the committee members reviewed the draft final regulation, further discussed the six major issues listed above, heard a presentation from a trade association on the potential inflationary impact of the GMP regulation, and discussed FDA's inspections surveying manufacturing practices in 300 device establishments, mentioned above. A transcript of this meeting is available at the office of the Hearing Clerk (HFA-305), FDA (Ref. 6).

These inspections were conducted under the following FDA Compliance Programs: "Inspection of Medical

Device Manufacturers" and "Inspection of Diagnostic Product Manufacturers" (Refs. 7 and 8). The report based on these inspections revealed that many device manufacturers were not meeting the proposed device GMP requirements, particularly proposed §§ 820.20 *Organization,* 820.80 *Components,* 820.120 *Device labeling,* and 820.130 *Device packaging.* Although it is important to recognize that this report may not be representtive of the device industry as a whole, the data suggest that a number of device manufacturers were not following important provisions of the proposed regulation that represent current good manufacturing practices. However, the majority of manufacturers complied with half or more of the proposed requirements.

In reviewing the final draft GMP regulation for devices, the committee suggested numerous editorial changes and made recommendations, summarized below, on the six major issues. The comments of other interested parties on these six major issues and the Commissioner's treatment of these comments are found under the heading "The Commissioner's Responses to the Public Comments," and appear below in this preamble.

1. *Effective date of the regulation.* The committee recommended that the final regulation be effective 180 days after publication and suggested that, during the 180-day period after the effective date, the agency exercise reasonable flexibility in implementing this regulation to allow for appropriate adjustments by industry and FDA.

The Commissioner agrees that industry should have a period of time following the publication of the regulation to allow for appropriate adjustments in manufacturing practice. The Commissioner has decided that it is appropriate for the regulation to be effective 150 days after publication. FDA's implementation philosophy is described under the heading "Implementation," which appears below in this preamble.

2. *Exemption or variance procedure.* The committee recommended that exemption or variance procedures be published in the final regulation. The committee felt that at the time the regulation was being promulgated, the affected industry should have the opportunity to seek exemptions or variances from those requirements which manufacturers felt were not appropriate to their manufacturing operations.

The Commissioner is adopting this recommendation by adding a reference to section 520(f)(2) of the act and 21 CFR 10.30 on citizen petitions to FDA as procedures for applying for exemptions or variances from device GMP requirements.

3. *Applicability to foreign manufacturers.* The committee expressed concern that the GMP regulation be applied to foreign manufacturers in a manner which would not result in discrimination against domestic manufacturers.

The Commissioner agrees that the device GMP regulation should apply to the manufacture of any device to be imported or offered for import into the United States. This was Congress' intent in amending section 801(a) of the act (21 U.S.C. 381(a)) to allow the Commissioner to prohibit the importation of a device that was not manufactured in conformance with the good manufacturing practice requirements. Devices that appear to be unsafe or ineffective, to have been manufactured under conditions that were not in compliance with the GMP regulation, or to be otherwise adulterated or misbranded will be detained when offered for import and will not be permitted to enter the United States until FDA is satisfied that these devices, and where possible the conditions under which they were manufactured, are in full compliance with the act and FDA regulations. FDA now inspects some foreign device firms and has plans to increase the number of foreign inspections. FDA is also exploring, with representatives of foreign countries, the possible development of bilateral agreements which will provide for the uniform application of GMP requirements and exchange of inspectional information on the manufacturing practices of domestic and foreign firms. These efforts recognize the importance of international uniformity of requirements so that foreign and domestic manufacturers both are treated fairly.

4. *Disclosure of internal audits.* The committee recommended that FDA not ask for a company's internal audits. The committee felt that internal audits would not be useful or meaningful to a firm's management as a self-inspection tool if the internal audit was available to FDA.

A discussion of the Commission's findings on FDA's access to internal audits is found under the heading "Organization and Personnel," which appears elsewhere in the preamble.

5. *Inflationary impact.*—The committee expressed concern about the costs to industry of implementing the regulations and the potential inflationary impact on the cost of health care. The committee suggested that FDA undertake a cost-benefit analysis 1 year after the effective date of the regulations to determine its impact on the cost of health care.

The Commissioner recognizes the legitimacy of the concerns about the cost of the regulation to industry and the general public. He specifically requested comments on this issue in the proposal. The Commissioner has placed an economic impact assessment of the final GMP rule on file for public review in the office of the hearing clerk (HFA-305), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857 (ref. 9).

Comments filed by affected industry members and other interested parties revealed that reliable quantitative data on expected economic impact of the regulation are not available and could not be readily developed in the near future. The agency tried to estimate the impact of the regulation based on data submitted by the industry, which is in the best position to assess the impact of the regulation on current practices. Although the data submitted by the industry were fragmentary, ambiguous, and not representative of the industry as a whole, the Commissioner believes that manufacturers' expressed concerns about the cost of complying with the regulation were legitimate and real. Chief concerns related to recordkeeping requirements; the need for increases in personnel; the requirement that the quality assurance unit be organizationally independent from production units; housing and content requirements for various files; the definition of the term "critical device"; the role of the inspector; and the appropriateness of applying umbrella provisions to individual segments of the industry that have their own characteristic needs. But most comments were more issue-oriented than cost-oriented and reflected a primary desire that particular provisions be revised, replaced, deleted, less ambiguously stated, or made less stringent. The Commissioner has responded to these issue-oriented comments below.

In reviewing the comments, in light of FDA's survey of 300 device establishments, the Commissioner notes that those industry segments which will have to increase their quality assurance expenditures the most to comply with the regulation also stand to gain the most from the regulation, in terms of lower cost, by avoiding device failures, recalls, and product liability. However, in estimating expenses, none of those who submitted comments gave any evidence of having factored in these potential savings. Nor did comments estimate the savings to society if defective devices, attendant injuries, and medical costs can be reduced by the regulation.

In developing the draft regulation, FDA made many changes in response to comments. These changes rendered obsolete some of the economic estimates contained in comments on the proposed regulation. To refine and update the submitted comments, FDA sent a questionnaire to all firms that

had commented on the potential economic impact, asking 14 questions based on specific parts of the regulation (ref. 10). FDA asked whether a change in a provision would alter the comment's previous assessment of economic impact. The questionnaire also asked commentors to determine the overall difference in cost of the regulation if all changes in the regulation were made.

FDA compared industry comments on inflation impact of the proposal with industry comments on inflation impact of the draft final regulation made publicly available on October 25, 1977. Commentors tended to scale down their original estimates, probably because changes in the draft final regulation would reduce compliance costs.

Because of the unavailability of a data base for estimating the cost impact of the regulation, the agency asked for such data from four quality assurance experts of the American Society for Quality Control. Since these four experts participated with FDA representatives in a series of conferences to inform the device industry of the provisions of the GMP regulation, they were very familiar with all of the requirements of the regulation. The cost estimates prepared by each of the quality assurance experts is summarized in the economic impact assessment on file in the office of the hearing clerk.

Factors which FDA hopes will reduce the regulation's costs include the flexibility provided in the document, the opportunity for manufacturers to petition for an exemption or variance from one or more requirements, the time given industry to comply with the regulation, and FDA's education and training programs for industry.

The Commissioner is confident that the costs imposed by the GMP regulation will be greatly outweighed by its benefits. Although he has no current plans to undertake the suggested cost benefit study of the impact of GMP regulation on the cost of health care, the Commissioner does intend to study the overall economic impact of the medical device amendments of 1976.

6. *Definition of a "critical device".*—The majority of committee members concluded that no one definition of the term "critical device" would be acceptable to all interested persons. Concern was expressed about the need to retain the term "user" found in the proposed definition rather than the term "patient," which appeared in the draft made available on October 25, 1977. Some members believed health professionals, such as doctors and nurses, as well as patients, should be considered when attempting to apply this definition and that the term "user" was descriptive enough to include both the patient and the health professional who use devices.

The Commissioner recognizes that it is difficult to define the term "critical device," but finds that the definition in the draft made available on October 25, 1977, is sufficient to communicate the concept of "critical device." However, the Commissioner will retain the term "user," which was in proposed § 820.3(f), because it is broader than the term "patient."

The Committee and many comments recommended that the agency develop a list of critical devices so that the industry and FDA field personnel will know what devices are subject to critical device requirements. The Commissioner agrees with the committee that a list of examples of critical devices should be developed and made available. The process used by FDA to develop this list and the involvement of the Device GMP Advisory Committee in this effort are described below.

Development of a Critical Device List

The Commissioner agrees with these comments and has developed a list of critical devices to serve as guidance to the industry. This list is available and will be provided to all critical device manufacturers who are registered with FDA and, upon request, to any other interested person.

In developing a list of critical devices, FDA used the following definition found in the draft final regulation: "a device intended for surgical implant into the body or to support or sustain life whose failure to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in a significant injury to the patient." FDA first compiled a list of devices based on preliminary findings and recommendations of FDA's device classification panels (ref. 11). The list includes those devices that the panels designated as life-sustaining or life-supporting and those devices that the panels had tentatively recommended for classification into class III (those for which premarket approval will be required).

After the August 4, 1977, meeting of the Device GMP Advisory Committee, FDA asked committee members to review the list and identify devices which should be deleted from it. During the October 27-28, 1977, committee meeting, the committee suggested some revisions in the definition of "critical device" and recommended that the agency consult with the device classification panels about which particular devices meet the revised definition, because the committee believed these panels have additional knowledge of particular devices. In addition, individual members of the Device GMP Advisory Committee provided the agency with additional recommendations on what should be included in the list.

The agency then prepared a revised list of critical devices, which it sent to one or more members of each device classification panel, with a request for recommendations about which devices should be added to or deleted from the list. Panel members were instructed to evaluate each possible critical device in light of the definition of "critical device" and their knowledge of, and experience with, the device.

In developing the list of critical devices, which appears below in this preamble, FDA has used the recommendations received from the Device GMP Advisory Committee and the device classification panels. This list of critical devices is based on the revised definition of "critical device" appearing in this regulation and on the most current information available to FDA. FDA will revise this list periodically, after consulting with the Device GMP Advisory Committee, as additional information becomes available. Revisions of the list will be announced in the Federal Register and will be available from the Bureau of Medical Devices, Division of Compliance Programs, 8757 Georgia Avenue, Silver Spring, Md. 20910. The Commissioner emphasizes that this list of critical devices is only illustrative and is being provided as guidance to the industry. The list is not intended to be definitive or exhaustive. Each manufacturer should refer to the definition of "critical device" in determing whether the critical device requirements apply to that manufacturer's device.

In accordance with the registration and listing requirments in 21 CFR Part 807, FDA will use the information submitted by manufacturers to generate a listing of all manufacturers who make identified critical devices. Once this information is compiled, FDA will notify each manufacturer of such a critical device that FDA has determined that the critical device GMP requirements apply to that device.

Guideline List of Critical Devices

1. Airway, Bi-Nasopharyngeal (with connector).
2. Airway, Esophageal (obturator).
3. Airway, Nasopharyngeal (with connector).
4. Airway, Oropharyngeal, Anesthesiology.
5. Analyzer, Oxygen, Neonatal Invasive.
6. Apparatus, Electronanesthesia.
7. Apparatus, Hemoperfusion, Sorbent.
8. Apparatus, Suturing, Stomach and Intestinal.
9. Autotransfusion Apparatus.
10. Balloon, Intra Aortic, and Control System.
11. Band, Tubal Occlusion.
12. Bed, Radiant Heat.

13. Blood Pump, Cardiopulmonary Bypass, Non-Roller.
14. Blood Pump, Cardiopulmonary Bypass, Roller Type.
15. Bypass, Ventricular (assist).
16. Catheter, Embolectomy.
17. Catheter, Intravascular Occluding.
18. Catheter, Septostomy.
19. Circuit, Breathing (w/connector, adaptor Y piece).
20. Clip, Aneurysm.
21. Clip, Tubal Occlusion.
22. Clip, Vascular.
23. Clip, Vena Cava.
24. Compressor, External, Cardiac Powered.
25. Connector, Airway (extension).
26. Counter-Pulsating Device, External.
27. Cuff, Tracheal Tube, Inflatable.
28. Defibrillator, DC-Powered (including paddles).
29. Detector and Alarm Arrhythmia.
30. Electrode, Pacemaker, Permanent and Temporary.
31. Filter, Intravascular, Cardiovascular.
32. Generator, Oxygen, Portable.
33. Generator, Pulse, Pacemaker, External.
34. Generator, Pulse, Pacemaker, External, Programmable.
35. Generator, Pulse, Pacemaker, Implantable.
36. Hemodialysis Systems (including accessories).
Dialyzers, Capillary Hollow Fiber.
Dialyzers, Disposable.
Dialyzers, High Permeability.
Dialyzer, Parallel Flow.
Dialyzer, Single Coil.
Dialyzer, Twin Coil.
Set, Dialysis, Single Needle.
Systems for Dialysate Delivery.
37. Incubator, Neonatal Ventilator.
38. Intrauterine Contraceptive Device (IUD) and Introducer.
39. Keratoprosthesis, Noncustom.
40. Lens, Intraocular, Ophthalmic.
41. Lung, Membrane (for long-term respiratory support).
42. Machine, Gas Anesthesia/Analgesia, Complete Systems.
43. Needle, Emergency Airway.
44. Oxygenator, Cardiopulmonary.
45. Pacemaker, Cardiac, External Transcutaneous.
46. Peritoneal Dialysis System, Automatic Delivery.
47. Prosthesis, Arterial Graft, Synthetic.
48. Prosthesis, Esophagus.
49. Prosthesis, Laryngeal.
50. Prosthesis, Trachea.
51. Prosthesis, Urethra Sphincter.
52. Prosthesis, Vascular Graft.
53. Pump, Infusion, Cardiovascular.
54. Pump, Withdrawal/Infusion.
55. Replacement, Urethral.
56. Respirator, Neonatal Ventilator.
57. Resuscitator, Cardiac, Mechanical.
58. Resuscitator, Pulmonary, Manual.
59. Shunt, Central Nervous System Fluid and Components.
60. Stimulator, Cerebella Implanted.
61. Stimulator, Diaphragmatic/Phrenic Nerve, Implanted.
62. Stimulator, Electroanesthesia.
63. Stimulator, Intracerebral/Subcortical Implanted (pain relief).
64. Suture, Cardiovascular.
65. Thromboemboli, Intravascular (artificial embolization device).
66. Tube, Bronchial (w/wo connector).
67. Tube, Tracheal (w/wo connector).
68. Tube, Tracheal/Bronchial, Differential Ventilation (w/wo connector).
69. Tube, Tracheostomy (w/wo connector).
70. Unit Emergency Oxygen and Resuscitation.
71. Valve, Heart Replacement.
72. Valve, Tubal Occlusion.
73. Ventilator, Continuous (respirator).
74. Ventilator, External Body, Negative Pressure, Adult (cuirass).
75. Ventilator, Noncontinuous (respirator).

THE COMMISSIONER'S CONCLUSIONS ON THE PUBLIC COMMENTS

FDA received approximately 140 written comments on the proposed regulation of March 1, 1977; these came from manufacturers, trade associations, professional associations, consultants, and other interested parties. Based on these comments, information provided at the public hearing held on August 5, 1977, and the recommendations of FDA's Device GMP Advisory Committee, FDA has made several changes in the final regulation. A discussion of the comments and changes follows:

GENERAL PROVISIONS

1. Several comments regarding the scope of the regulation in proposed § 820.1 said the GMP regulation should apply only to finished device manufacturers because manufacturers of components may supply only a fraction of their production to finished device manufacturers. In addition, it was suggested that components, e.g., transistors, semiconductors, etc., for many finished devices are readily available in the marketplace and are not manufactured exclusively for use in devices. Several comments argued that devices would be more costly if device component suppliers have to comply with the GMP regulation.

The Commissioner agrees with the comments and has amended the final regulation to apply to manufacture of finished devices only. Although the regulations do not apply to component suppliers, the Commissioner has required manufacturers of finished devices to take the necessary precautions to assure the quality of components. He also encourages component manufacturers to use the regulations as a guide where appropriate.

The Commissioner points out that manufacturers of human blood and blood components are subject to requirements of 21 CFR part 606 and not to part 820. A statement to this effect has been added to § 820.1.

2. Many comments suggested deletion of the reference to "installation of devices" in proposed § 820.1 *Scope*, because most devices are not installed by the manufacturer.

The Commissioner rejects this suggestion because some devices must be installed by the manufacturer or other qualified person before they can be used. A new § 820.152 *Installation* is added to the final regulation to recognize the importance of installation to the proper functioning of a device. Section 820.152 of the final regulation requires that where a device is installed by the manufacturer or the manufacturer's authorized representative, the manufacturer or representative shall inspect the device after installation to assure that it performs as intended. Where a device is installed by a person other than the manufacturer or an authorized representative, the manufacturer is required to provide adequate instructions and procedures for proper installation.

3. Several comments suggested that only firms required to register with FDA be required to comply with the regulation.

The Commissioner disagrees with this suggestion because some firms are exempted from the requirement to register for reasons which do not relate to the need to comply with GMP requirements. Therefore, it would be inappropriate to exempt categorically these firms from GMP requirements. For example, foreign manufacturers are not required to register, but shall be required to meet GMP requirements.

4. Several comments said the proposed regulation did not represent "current" practice and recommend deleting the term.

The Commissioner disagrees with this recommendation because the regulation is designed to reflect present good industry practices and provides the type of flexibility necessary to allow for changes to reflect advances in technology and new manufacturing procedures. Many changes were made in response to comments on the initial draft and to the published proposal to address the concerns of industry as to the currentness of this regulation.

5. Several comments suggested that business firms be included in the subparagraph on authority in proposed § 820.1(a). A few of these comments suggested that the word "manufacturer" be substituted for "person."

The Commissioner rejects these comments because "person" in this sense, and as defined in section 201(e) of the act (21 U.S.C. 321(e)), includes individuals, partnerships, corporations, and associations.

6. Several comments objected that the regulation does not make special provisions for minor violations.

The Commissioner rejects these comments because he believes they are not pertinent to the proposed regulation. The Commissioner will determine on a case-by-case basis which violations of the regulation are minor and the type of regulatory followup neces-

sary to effect compliance, as the Commissioner is permitted to do under section 306 of the act (21 U.S.C. 336).

7. Several comments on proposed § 820.1(b) *Limitation* said that because in vitro diagnostic (IVD) products are now devices, the drug GMP regulation should no longer apply to the manufacture of IVD's. The comments suggested that § 809.20(b), which now requires manufacturers of these products to follow the drug GMP regulation as a guideline, should be modified.

The Commissioner agrees with the comments because this regulation applies to all devices, including IVD products. The Commissioner is amending § 809.20(b) to state that IVD manufacturers shall comply with the device GMP regulation.

8. Many comments urged clarification of the applicability of the GMP regulation to foreign manufacturers of devices offered for importation into the United States. Some of the comments said that unless FDA plans to inspect such foreign manufacturers, there is no way the agency can effectively regulate imports.

The Commissioner rejects these comments because FDA will continue its longstanding practice of inspecting foreign plants and plans in the future to conduct more inspections of foreign manufacturers of devices offered for importation into the United States. Such foreign manufacturers, like domestic manufacturers, are required to comply with the GMP requirements. Any imported device about which the agency has questions with respect to safety and effectiveness will be detained upon importation until the agency is satisfied that it complies with all applicable laws and regulations administered by FDA. In addition, FDA will attempt to develop and implement bilateral agreements with appropriate Government officials in other countries to provide greater assurance that foreign manufacturers of devices offered for importation into the United States are adhering to the GMP regulation.

9. Several comments said the proposed regulation should be clarified to provide that device GMP regulations are meant to apply to devices intended for human use only.

The Commissioner finds it unnecessary to clarify the regulation because proposed § 820.1 *Scope* expressly limits the regulation to devices intended for human use.

The Commissioner has revised proposed § 820.1 by moving to new § 820.5 *Quality assurance program* the requirement that every device manufacturer shall prepare and implement a quality assurance program that is appropriate to the specific device manufactured and that meets the requirements of this regulation. The Commissioner is making this change to emphasize the importance of this requirement.

DEFINITIONS

10. One comment suggested deleting the proposed definition for "automated quality control" since this activity was adequately covered by the proposed definition of "quality control unit."

The Commissioner has deleted the definition of "automated quality control" from the final regulation because this term is adequately described in the definition of "quality assurance" and in § 820.20(a). Additionally, the term "quality control" is replaced throughout the regulation with the term "quality assurance" to reflect suggestions provided in the comments and the Commissioner's belief that the term "quality assurance" is broader and more precise than the term "quality control."

11. Several comments suggested changes in the proposed definition of "component" to clarify the meaning of the phrase "will appear." Many comments said the reference to "appearing" raised questions about whether components which are not visible in the finished device are covered.

The Commissioner agrees with the comments, and the definition of "component" is amended in the final regulation to state that "component" means any material, substance, piece, part, or assembly used during device manufacture that is intended to be included in the finished device.

12. Many comments suggested changing the proposed definition of "control number" to reflect the current industry practice of using letters, numbers, or both.

The Commissioner agrees with the suggestion to allow letters and/or numbers, and the definition is changed accordingly.

13. Several comments on the proposed definition of "control number" suggested adding a provision for the use of symbols or other markings as well because it may not be practical to use only numbers and letters.

The Commissioner is not persuaded that there is any need for the use of symbols and other markings other than letters and/or numbers, and he is not making the requested change.

14. Many comments said the proposed definition of "critical component" was too broad and could be construed to mean any component in a critical device.

The Commissioner agrees, and the definition of "critical component" is revised in the final regulation to include any component whose failure to perform can be reasonably expected to cause the failure of a critical device or to affect its safety or effectiveness.

15. Many comments suggested that the proposed definition of "critical device" be revised to identify more accurately those characteristics of a device which require that it be considered a critical device. It was stated that the proposed definition could be misinterpreted to encompass certain types of devices that the comments do not believe the Commissioner intended to be regarded as critical.

The Commissioner is changing the definition of "critical device" in the final regulation to include only those devices intended for surgical implant into the body or to support or sustain life, whose failure to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in significant injury to the user.

16. Many comments indicated that the 19 device advisory classification panels, rather than the Device GMP Advisory Committee, should either decide or be consulted on which devices are critical and which are not.

The Commissioner consulted with the device advisory classification panels in developing the initial list of examples of critical devices. However, the Commissioner finds that the members of the Device GMP Advisory Committee are competent to make recommendations as to which devices are critical. Therefore, the regulation provides for the Commissioner to consult with the Device GMP Advisory Committee before identifying critical devices. The process FDA used in identifying examples of a critical devices is described under the heading "Development of a Critical Device List," which appears elsewhere in this preamble.

17. Several comments said only class III devices (those requiring premarket approval) should be declared "critical."

The Commissioner disagrees because some life-supporting or life-sustaining devices will not be subject to class III controls, but rather will be subject to class II controls (devices requiring standards).

18. Several comments said the term "implant" in the proposed definition of "critical device" should be defined.

The Commissioner disagrees, because any decision to determine whether a device is "critical" will not depend entirely on its being an implant. In addition, the Commissioner has proposed a definition of the term "implant" in the proposed regulation on device classification procedures published in the FEDERAL REGISTER of September 13, 1977 (42 FR 46028).

19. Several comments said the proposed definition of "critical device" should reflect the fact that critical devices may replace or assist nonfunctioning organs. A few comments suggested that support of life

be differentiated from sustenance of life.

The Commissioner rejects the comments because devices that replace body organs should be treated on a case-by-case basis in determing whether such devices are life-sustaining or life-supporting. The Commissioner believes that if a device fails while it is in use by or on any person, and if such failure can be reasonably expected to result in death or a clearly diminished capacity to function as an otherwise normal human being, then that device is life-sustaining or life-supporting.

20. Several comments said the condition of the patient at the time a device is used should be a factor in considering whether a device should be considered as a "critical device."

The Commissioner rejects the comments because the diagnosis of the "condition of the patient" is not pertinent to determing whether a device should be regarded as "critical" for purposes of applying the GMP regulation. The state of health of the patient is a medical judgment or diagnosis made by physicians and health professionals. The criticality of a device under this regulation depends on characteristics of the product, i.e., that the device sustains or supports life. The suggestion that FDA take into account the condition of the patient in defining "critical device" is impractical and unworkable because use of this additional criterion would make it impossible for a manufacturer to identify critical devices.

21. Several comments proposed that the definition of "critical device" reflect the fact that user error accounts for many device-related patient injuries.

The Commissioner agrees with these comments, and the definition in the final regulation is modified to recognize the relevance and importance of using a device in accordance with instructions provided in the labeling.

22. One comment recommended that dental implants be included in the definition of "critical device" in proposed § 820.3.

The Commissioner disagrees with the comment because dental implants that should be considered "critical" would be adequately covered by the term "implant" and the other criteria contained in the definition of "critical device."

23. One comment said the "permanent injury" referred to in the proposed definition of "critical device" should be more clearly defined.

The Commissioner is substituting "significant injury" for "permanent injury" because he believes "significant injury" is more descriptive of that type of hazard that requires the application of critical device GMP controls to provide protection to the public.

24. Many comments objected to the proposed definition of "critical device" on the ground that the definition could be interpreted to allow the Commissioner to ignore the criteria for determining the criticality of a device and arbitrarily designate certain devices as critical. The comments suggested that the Commissioner should be subject to the "definitional limitations" or criteria contained in the definition in designating critical devices.

The Commissioner never intended to suggest that he could ignore the criteria and arbitrarily designate any device as "critical." Accordingly, the Commissioner is amending the final regulation to clarify this point. A new sentence describing the Commissioner's role in the identification of critical devices is added to the definition: "Critical devices will be identified by the Commissioner after consultation with the Device Good Manufacturing Practice Advisory Committee authorized under section 520(f) of the act, and an illustrative list of critical devices will be available from the Bureau of Medical Devices, Food and Drug Administration."

25. Several comments said the definition of "critical operation" in proposed § 820.3(g) was too broad because it could be interpreted to mean that all manufacturing operations relating to a critical device were critical operations.

The Commissioner agrees that the definition should be clarified. The Commissioner is revising the definition to mean any operation in the manufacture of a critical device which, if improperly performed, can be reasonably expected to cause the failure of a critical device or to affect its safety or effectiveness.

26. Many comments concerning the definition of "finished device" in proposed § 820.3(h) (now § 820.3(j)) suggested that the phrase "whether packaged or labeled for commercial distribution" should be deleted because a device is not a "finished device" until it is packaged and labeled.

The Commissioner disagrees with the comments because some manufacturers make devices that are packaged and/or labeled by other firms. In these instances the regulation applies to both the person manufacturing the device and the person repackaging or relabeling the device.

27. Many comments objected to the definition of "manufacturer" in proposed § 820.3(i) (now § 820.3(k)), which included any person who manufactures, fabricates, assembles, or processes a device in "whole or in part". Comments said this provision was too broad, particularly in the instance of suppliers (vendors) who provide general-use components to manufacturers who use such components as parts of devices.

The Commissioner agrees with the comments, and he is revising the regulation to define "manufacturer" to mean any person, including any repacker and/or relabeler, who manufacturers, fabricates, assembles, or processes a finished device. The term does not include any person who only distributes a finished device.

28. Several comments said the proposed definition of "manufacturer" should be modified to eliminate the possibility that a manufacturer might be held responsible for devices altered without the manufacturer's knowledge.

The Commissioner advises that the definition was not intended to suggest that Part 820 would make a manufacturer responsible for changes in devices by others, after the device left the manufacturer's control. However, he believes that no change in the definition of "manufacturer" is necessary.

29. Several comments suggested including definitions of the following terms: "audit," "controlled label," "device history record," "documented," "inspection," "master device record," "non-critical component," "quality assurance," "quality assurance program," "quality program," "quality control," and "quality control manual."

The Commissioner agrees in part and has determined that the regulation can be more easily understood if the terms "audit," "device history record," "device master record," and "quality assurance" are defined. Accordingly, the final regulation is amended to include definitions of these terms. The definitions for the terms "audit" and "quality assurance" have been adapted from the "Working Draft on Quality Systems Terminology" (ref. 12). The Commissioner has determined that the other suggested terms do not require a definition since the meanings provided by a dictionary are sufficient.

The Commissioner notes that the term "finished device" is used in §§ 820.1, 820.3, and 820.5 to clarify the intent of the regulation. Wherever the term "device" is used elsewhere in Part 820, it should be understood to mean "finished device."

Organization and Personnel

30. Many comments on proposed § 820.20 *Organization* said the requirement that the quality control unit be organizationally independent of, or separate from, units performing the manufacturing operations was overly restrictive and unduly burdensome to small device manufacturers. They argued that small manufacturers would be forced to hire additional per-

sonnel because it is common practice in a small company for the same individual to perform both a quality assurance and a production function. Other comments said FDA should not concern itself with the organizational structure of a company because the structure has nothing to do with good manufacturing practices.

The Commissioner is revising the requirement that a manufacturer have in its organization a quality assurance unit that is organizationally independent of, or separate from, units performing manufacturing operations. The regulation now requires that each manufacturer prepare and implement quality assurance procedures to assure that a formally established and documented quality assurance program is performed. After reflecting on the concerns raised by small manufacturers on the implications of organizational requirements, the Commissioner has determined that it would be unwise at this time to mandate that each manufacturer have a separate quality assurance unit. In making this change, the Commissioner recognizes that effective quality assurance procedures depend more on the commitment of top management to exercise leadership in planning, designing, implementing, and assessing the quality assurance program than on the establishment of a separate quality assurance unit. Although many manufacturers have determined that an objective and accountable quality assurance process can be achieved most effectively by establishing an independent quality assurance unit, the Commissioner believes the desirable objectivity and accountability can be achieved without dictating organizational requirements. FDA is more interested in the adequacy and appropriateness of the quality assurance program that each manufacturer has developed than in the organizational structure of the company.

Because the regulation no longer requires each manufacturer to have in its organization a quality control unit, the Commissioner finds it unnecessary to define the term "quality control unit," and he has deleted the definition from the final rule.

The Commissioner has also amended the regulation to provide that, where possible, a designated individual(s) not having direct responsibility for the performance of a manufacturing operation shall be responsible for the quality assurance program. Although production and quality assurance personnel share a common goal of assuring that high quality devices are produced, their interests may sometimes conflict in the short run as decisions are made that will affect a company's output. The Commissioner has used the words "where possible" in this requirement because he recognizes that for very small companies (one or two employees) it would be impossible for the designated quality assurance individual not to have responsibility for a production function.

31. Several comments said individual employees should be able to check and verify their own work. They argued that if such checks are not done by the employees themselves, a production foreman or supervisor should perform them, because these individuals are more familiar with the manufacturing operations than is an independent quality control person.

The Commissioner never intended that production personnel should not be able to check or inspect their own work. Checking and inspection activities are highly desirable and help to assure that devices are fit for their intended use. But adherence to an adequate quality assurance program provides a further check to assure that material and production specifications are met. In an effective quality assurance program, the checking and inspection for adherence to specifications that are done by production and quality assurance personnel alike complement one another and provide greater assurance that high quality devices are produced.

32. Several comments on proposed § 820.20 suggested that the term "quality control" be changed to "quality assurance" since the latter term is more inclusive and familiar in industry.

The Commissioner agrees with the suggestion, and § 820.20 is changed accordingly. The Commissioner has changed the term "quality control" to "quality assurance" wherever the term appears in the final regulation.

33. Several comments on the proposed responsibilities of the quality control unit under § 820.20(a) said manufacturers should be responsible only for those devices they manufacture and not for those manufactured for them by other firms under contract.

The Commissioner disagrees with the comments and believes a manufacturer should have adequate control measures designed and in force to assure that any firm manufacturing a device for it under contract complies with the GMP regulation.

34. Several comments said the quality control unit need not check in-process production of noncritical devices because it has the authority to reject the finished device if that should prove necessary.

The Commissioner disagrees with these comments because he has not mandated any in-process checks during the production of noncritical devices. It is the manufacturer's responsibility under § 820.5 to determine whether such checks are necessary for the production of noncritical devices. Through inspections, FDA will review these management decisions and quality assurance procedures and communicate to the firm its observations on the adequacy of, and the adherence to, a manufacturer's procedure for in-process checks.

35. Several comments said the quality control personnel have no need to review production records, as these records have no bearing on the quality of the device.

The Commissioner disagrees. An effective quality assurance program requires a careful and periodic review of all elements of manufacturing practice that have a bearing on the quality, safety, and effectiveness of a device. A careful review includes the verification and evaluation of each quality factor that affects production to assure that all processing and performance specifications are met. A review of production and other records by quality assurance personnel is fundamental to the implementation and maintenance of an effective quality assurance program. The review of production records provides management with feedback on the results of the production activity and with assurance that production, process, and performance specifications are being met.

36. Several comments urged that the requirements of the quality control function, as stated in proposed § 820.20(a), be clarified.

The Commissioner agrees, and § 820.20(a) is revised to clarify the requirements of the quality assurance program.

37. Many comments expressed reservations about proposed § 820.20(b), which requires audits of a manufacturer's quality assurance program. These comments objected to any provision that would require the disclosure of internal audit reports to FDA. It was stated that any requirement which would result in disclosure of internal audit reports would lead to a weakening of the audit system because firms would be reluctant to be candid when expressing in writing the results of their internal audits if this information were freely available to FDA and to the public under the Freedom of Information Act. It was further argued that concern about self-incrimination would result in the preparation of "sanitized" audit reports. A few comments suggested that, if procedures for internal audits are required, firms should have the flexibility to provide FDA with complete summaries of the outcome of an audit and any decision resulting from observations uncovered during the audit. It was further stated that a summary should be sufficient to enable FDA to determine whether audits have been performed and to

verify that appropriate action was taken by management.

The Commissioner believes that planned and periodic audits of quality assurance should be undertaken because the maintenance of a useful quality assurance program requires that the program be subjected to periodic review. In addition, the proper implementation of an audit system for quality assurance can result in cost-savings to the manufacturer if problem areas are identified and corrected.

The Commissioner shares the concerns of the comments and the Device GMP Advisory Committee that general FDA access to audit reports would tend to weaken the audit system. He believes that auditing of quality assurance programs is important, and he recognizes the need to maintain a degree of confidentiality if audits are to be complete and candid. Therefore, the Commissioner has decided that FDA must require each manufacturer to conduct periodic audits of its quality assurance program and to prepare audit reports. The Commissioner has also concluded that FDA must routinely inspect and copy manufacturers' internal audit procedures. However, as a matter of administrative policy, FDA will not request inspections and copying of the reports of audits of a manufacturer's quality assurance program when FDA conducts routine surveillance of a manufacturer's compliance with device GMP's. When FDA needs to determine whether a manufacturer is conducting audits in accordance with the regulation, a designated FDA employee may request a responsible official of the manufacturer to certify in writing that the manufacturer has complied with § 820.20(b). Upon receiving such a request, the official is required to submit, or to have another responsible official of the manufacturer submit, the certification of compliance. A person who submits a false certification is liable to prosecution under 18 U.S.C. 1001 and 21 U.S.C. 331(q)(2).

The one exception to FDA's policy of not seeking access to reports of audits of quality assurance programs is that FDA may seek production of these reports in litigation under applicable procedural rules, as for other otherwise confidential documents.

It should be stressed that FDA's policy of not generally seeking access to audit reports applies only to reports of periodic audits (as defined in § 820.3(b)) of a manufacturer's quality assurance program, not to any records concerning particular devices or any other records concerning quality assurance or production. Records required under other sections of part 820, e.g., §§ 820.161 on finished device inspection, 820.162 on failure investigation, and 820.198 on complaint files, are subject to routine FDA inspection and are not governed by the policy in § 820.20(b) concerning FDA access to audit reports.

38. Many comments on proposed § 820.25 *Personnel* said the requirement that personnel have adequate educational background, training, and experience was too restrictive and that the phrase "qualifications and experience" was sufficient.

The Commissioner disagrees with these comments because the stated requirements are not too restrictive. The requirement of "sufficient personnel with the necessary education, background, training, and experience to assure that all manufacturing operations are correctly performed" is a flexible one. In the Commissioner's opinion the suggested term "qualifications" would include education, background, and training.

39. Many comments said training programs in proposed § 820.25(a) need not be documented and such documentation would create unnecessary paperwork and expense without achieving any significant benefit.

The Commissioner disagrees with the comments, but § 820.25(a) is revised in the final regulation to require that all personnel have the necessary training to perform their assigned responsibilities, but only to require documented training programs where such programs are necessary to assure that personnel have a thorough understanding of their jobs. He believes it is essential that the manufacturer formally recognize any training required for the performance of specific work by its employees. Where no training programs are necessary, the manufacturer is not required to implement an unnecessary program.

40. Many comments objected to the requirement in proposed § 820.25(a) that a documented training program be in effect for quality control personnel regarding defects and errors likely to be encountered in their individual control functions.

The Commissioner agrees with these comments, and § 820.25(a) is revised in the final regulation to eliminate the need for a documented training program on defects and errors for quality assurance personnel. However, he is revising and expanding this section to require manufacturers to strive for "defect awareness" by all employees. The final regulation requires that all employees be made aware of device defects that may occur from the improper performance of their specific jobs. Quality assurance personnel shall be made aware of defects and errors likely to be encountered as part of their individual quality assurance function.

41. Many comments said on-the-job training was more effective than a documented training program and best served to provide the necessary experience required by the regulation.

The Commissioner recognizes the value and desirability of on-the-job training programs and advises that § 820.25(a) in the final regulation allows for such training.

42. Several comments concerning the personnel health and cleanliness requirements in proposed § 820.25(b) said this provision should apply to sterile device manufacturers only.

The Commissioner disagrees with the comments because devices other than sterile devices, e.g., diagnostic products, may be adversely affected by poor personnel health and cleanliness practices. However, he points out that the requirement applies only to the extent that the cleanliness, health, and attire of personnel in contact with the device or its environment may affect the device.

43. Several comments said proposed § 820.25(b), concerning personnel health and cleanliness, was under the purview of the Occupational Safety and Health Administration, not FDA.

The Commissioner disagrees with the comment and has determined that the Occupational Safety and Health Act (OSHA) regulations do not include all of the personnel health and cleanliness requirements needed in this regulation, which aims at protecting device users from defective devices rather than protecting manufacturing employees from job-related hazards. Although there are some areas of common interest, the Commissioner believes that this regulation does not conflict with OSHA regulations.

BUILDINGS

44. Many comments objected to the use of the word "prevent" in proposed § 820.40 *Buildings* in the provision that facilities provide adequate space to prevent mixups, and in other parts of the proposal. The comments agreed that "prevent" is an absolute and connotes an unattainable goal. The comments suggested that the term "prevent" be changed to "designed to prevent."

The Commissioner agrees with the suggestion, and the final regulation is changed accordingly.

45. Several comments objected to the requirement in proposed § 820.40 that buildings in which manufacturing, assembling, packaging, packing, holding, testing, and labeling operations are conducted shall be of suitable design and contain sufficient space to facilitate adequate cleaning, maintenance, and other necessary operations. It was argued that these requirements should apply only when the device itself may be affected if a building were improperly designed or

too crowded. The comments also said the requirement was too specific.

The Commissioner rejects the comments because the failure to have a suitably designed building with ample space for necessary operations may affect the safety and effectivness of virtually any device. The requirements that buildings be of suitable design and that buildings and facilities contain sufficient space to facilitate necessary operations and orderly handling of manufacturing operations provide manufacturers with flexibility and permit them to take into account the differences among various kinds of devices.

46. Several comments objected to the proposed requirement in § 820.46 that periodic verification of environmental controls be performed and documented. Comments suggested that verification implies documentation and that use of the word "documented" was redundant.

The Commissioner disagrees with the comments because verification can occur without documentation. Therefore, he believes it is necessary that any verification of environmental controls be documented and available for review.

47. Several comments suggested that verification of environmental control for noncritical device manufacturers, as proposed in § 820.46, was unnecessary. The comments further suggested that the requirements for the control of environmental conditions are too specific and that environmental conditions should be controlled only when they could affect the device.

The Commissioner rejects these comments. The proposed requirement already stated that environmental conditions shall be controlled when necessary, thereby allowing flexibility with respect to whether environmental conditions are to be controlled and, if so, the type of control applied. The Commissioner is clarifying § 820.46 to provide that environmental conditions at the manufacturing site shall be controlled when such conditions could have an adverse effect on a device's fitness for use.

48. Several comments recommended that the requirement in proposed § 820.56 that cleaning and sanitation procedures be adequate to meet process requirements apply only when necessary.

The Commissioner rejects the comments because adequate cleaning and sanitation procedures to meet process requirements are basic requirements of good manufacturing practice and are necessary to assure the safety and effectiveness of devices.

49. Several comments objected to the inclusion of proposed § 820.56(a) concerning personnel sanitation requirements. The comments contended that the need for personnel sanitation is obvious and is often assured by State and local laws.

The Commissioner disagrees with the comments. He does not believe that the need for personnel sanitation is universally understood. Moreover, no evidence was provided to establish that State and local laws generally require that adequate sanitation facilities be present in device establishments.

50. Several comments objected to the requirement in proposed § 820.56(b) that there be written procedures to prevent contamination and otherwise control vermin, pests, and insects.

The Commissioner rejects the comments because it is of utmost importance that devices be manufactured under clean, sanitary, and pest-free conditions.

51. Several comments suggested that requirements in proposed § 820.56(b) of procedures to control vermin, pests, and insects, and to provide safeguards to prevent contamination by rodenticides, insecticides, fungicides, fumigants, and hazardous substances should apply only where appropriate. Some of these comments said the documentation of procedures to control vermin, pests, and insects was unnecessary.

The Commissioner disagrees with these comments. He believes that documented procedures to control vermin, pests, insects, and chemical contaminants are necessary and appropriate for any device manufacturer.

52. One comment recommended deletion of the requirement concerning sewage and refuse disposal on the ground that this provision was adequately covered by local laws.

The Commissioner rejects the comment because not all local laws adequately address sewage and refuse disposal in device establishments.

53. Many comments suggested that the requirement for written procedures and schedules in proposed § 820.56(e) be prefaced by "when necessary" because not all cleaning procedures require written procedures and schedules.

The Commissioner disagrees because written procedures and schedules are generally necessary to assure that cleaning and sanitation procedures are in place. The Commissioner notes that the requirements of proposed § 820.56(e) have been incorporated into the introductory paragraph of § 820.56 on cleaning and sanitation.

EQUIPMENT

54. Several comments suggested deletion of the sentence in the introductory text of proposed § 820.60, which reads: "All manufacturing materials or other substances used with such equipment or which may come in contact with the device shall not adversely affect the device," since paragraph (d) of the same section makes it redundant.

The Commissioner agrees with the comments, and the sentence is deleted from the final regulation.

55. One comment regarding the requirements in proposed § 820.60, that equipment be designed to facilitate maintenance, adjustment, and cleaning, noted that manufacturers have no direct control over the design and specifications of the equipment they buy.

The Commissioner disagrees with the comment because equipment design and specifications can be detailed in a purchase agreement where necessary. In other cases, the manufacturer can exercise control over the suitability and acceptability of any equipment the manufacturer intends to buy.

56. Several comments argued that the requirement in proposed § 820.60(a) that schedules be visibly posted on or near each piece of equipment was impractical for many pieces of equipment and did not serve as an effective control function.

The Commissioner agrees that posting schedules is not always practical, but emphasizes that § 820.60(a) provides flexibility in that schedules need not be posted on equipment if they are readily available to personnel performing maintenance activities.

57. One comment argued that cleaning and/or adjustment may be necessary many times during the day for certain equipment and is routinely performed by operators as part of their jobs. Documenting these activities as required in proposed § 820.60(a) would add to costs without providing any benefits.

The Commissioner disagrees with the comment because he believes it is important that cleaning and adjustment be documented to insure that the equipment is operating properly and within stated tolerances. However, the regulation provides flexibility by allowing the manufacturer to determine how the documentation requirement should be applied to a piece of equipment that is cleaned or adjusted many times during a day. Proposed § 820.60(a) is rewritten to clarify its intent.

58. Many comments argued that inspections of regularly scheduled maintenance of all equipment as required in proposed § 820.60(b) is unnecessary. It was suggested that the phrase "where applicable" preface the requirement.

Although the Commissioner has not adopted the specific suggestion in these comments, he has revised the final regulation to clarify that periodic

documented inspections are required only for equipment subject to applicable maintenance schedules.

59. Several comments objected to the requirement in proposed § 820.60(c) that any inherent limitations or allowable tolerances be posted. Comments argued that this posting may be impractical since this information is a function of material, operation, tool size, speed, feed, and other factors. Comments suggested that this information on inherent limitations and allowable tolerances be allowed to be readily available rather than visibly posted.

The Commissioner accepts the comments, and the regulation is changed to allow any inherent limitations or allowable tolerances to be visibly posted on or near equipment requiring periodic adjustment, or to be readily available to personnel performing that function.

60. Many comments suggested that the requirement in proposed § 820.60(d), for documenting the use and removal of manufacturing materials, be limited to critical devices and critical components because such documentation is unnecessary for noncritical devices.

The Commissioner rejects the comments because some manufacturing materials left on a device, such as cleaning agents and lubricating oils, may adversely affect performance of a finished device regardless of whether the device is critical or noncritical. However, the final regulation only requires documentation of the removal, and not the use, of a manufacturing material.

61. Several comments noted that for many manufacturing materials it would be impractical to limit such materials to a specified amount as required in the proposal.

The Commissioner rejects the comments and points out that the manufacturer has flexibility in specifying levels of materials allowed on the device, provided the safety and effectiveness of the device are not compromised. The requirement directs the manufacturer to develop and follow his own procedures for limiting amounts of manufacturing materials. The Commissioner has revised this section to require that the procedures for the removal of manufacturing materials be in writing to assure that proper attention is directed to this activity.

62. Many comments said proposed § 820.61 *Measurement equipment;* § 820.62 *Critical devices, measurement equipment;* and § 820.68 *Equipment calibration* were redundant and resulted in needless duplication. It was suggested that these proposed sections be consolidated to eliminate inconsistent terminology and duplication.

The Commissioner agrees with the comments and the requirements of these proposed sections are consolidated into § 820.61 *Measurement equipment.* There are no specific requirements for critical device measuring equipment in the final regulation because the Commissioner believes that all measurement equipment should be properly calibrated and maintained, regardless of the type of device being manufactured.

63. Several comments said documented periodic inspection as required in proposed § 820.61 should not be required for all measurement equipment. Concern was also expressed about the frequency with which such equipment should be inspected.

The Commissioner disagrees with the comments. However, this section is revised in the final regulations so that the manufacturer shall have procedures that describe when measurement equipment is to be routinely calibrated, inspected, and checked. The calibration, inspection, and checking activities should be carried out as often as necessary to assure that the equipment is performing properly, and these activities are required to be documented.

64. Several comments said it is not always possible to attach a calibration record to each piece of measuring equipment as required in proposed § 820.68(b).

The Commissioner agrees and has amended the final regulation in § 820.61(c) to require that the necessary calibration records be displayed or readily available for each piece of equipment requiring calibration.

65. Several comments objected to proposed § 820.68(e), which required a designated individual to maintain a separate record showing calibration dates, methods, data, and by whom calibrated. It was suggested that this requirement is unnecessary since the individual actually performing the calibration is already required to document this activity.

The Commissioner agrees, and § 820.61(c) of the final regulation is revised to eliminate the need to maintain duplicative records of calibration.

66. Several comments stated that it is not always practical to trace a calibration standard to the national standards at the National Bureau of Standards (NBS), as required in proposed § 820.62. One comment suggested that the calibration of measuring equipment used in testing shipping cartons does not have to be traceable to any national standard.

The Commissioner agrees and is changing the final regulation in § 820.61(b) to provide that calibration standards shall be traceable to the national standards at NBS only where practical. The Commissioner is also amending the requirement to apply to noncritical as well as critical devices because he believes measurement equipment used to produce noncritical devices should also be carefully calibrated, where practical, with national standards to assure accuracy of any measurement operation.

Control of Components

67. Several comments suggested that the requirement in proposed § 820.80(a) for acceptance of components be limited to components requiring testing.

The Commissioner disagrees with the comments because appropriate procedures should be implemented to assure that all components are examined prior to acceptance. In some cases, the examination of components may be visual to verify that what was ordered has actually been received. For other components, detailed testing may be necessary.

68. Many comments objected to the requirement in proposed § 820.80(a) that only a designated individual could accept or reject components and said this implied that only one named individual could perform this function.

The Commissioner notes that he never intended that the term "designated individual" limit a task or operation to only one named individual. A firm may designate more than one individual to perform this function. This is true wherever the term "designated individual(s)" is used in the regulation.

The purpose of any requirement that a firm designate one or more individuals to perform a function is to insure accountability for that function.

69. Many comments noted that visual examination of each shipping container, as required in proposed § 820.80(a), is not feasible and suggested revising the statement to require inspections of each shipment.

The Commissioner rejects the suggestion because there is no indication that such visual observation would impose an undue burden on the manufacturer. If a large number of shipping containers are combined in pallet form, it may be sufficient to examine visually the outside containers as representative of the entire pallet and then undertake visual examination of individual shipping containers when the pallet is separated.

70. One comment said proposed § 820.80(a) should not require incoming testing and acceptance of standard electronic components.

The Commissioner believes that components should be inspected, sampled, and tested for conformance to specifications wherever deviations from component specifications could result in a device being unfit for its in-

tended use. This requirement is rewritten to clarify its intent.

71. Many comments suggested clarification of the requirement in proposed § 820.80(b) for records "of all obsolete and rejected components." One comment suggested that a requirement of records "of the disposition of obsolete or rejected components" would state more clearly the intent of this provision.

The Commissioner agrees, and § 820.80(b) is revised accordingly.

72. Several comments suggested that the stock rotation requirement in proposed § 820.80(b) apply only where needed because some products do not require rotation.

The Commissioner agrees with the comments, and the paragraph is rewritten to clarify his intention that those components whose fitness for use or quality deteriorates over time shall be stored in a manner to facilitate proper stock rotation.

73. Several comments objected that the word "obsolete" is inappropriate in proposed § 820.80(b) because obsolete components are often retained as spare parts.

The Commissioner rejects the suggestion because he believes that components used as spare parts are not really obsolete, as these components will be used to repair or recondition certain devices. The manufacturer should maintain a record of the disposition of all obsolete or rejected components, including those that are discarded, but not those used as spare parts. This paragraph is revised to clarify the intent of the requirement.

74. Many comments objected to the requirement in proposed § 820.81(a) that an individual be designated to maintain rejection percentages for all critical components and said the availability of raw data on rejection records for critical components was sufficient.

The Commissioner agrees with the comments, and the requirement for a designated individual to maintain rejection percentages for critical components is deleted from § 820.81(a). Additionally, the final regulation clarifies that all lots of critical components shall be representatively sampled for testing and examination. The Commissioner believes this requirement is necessary to assure that critical components are fit for their intended use.

75. Several comments argued that the requirement in proposed § 820.81(a) that a control number be used to identify critical components upon receipt was unnecessary.

The Commissioner disagrees with the comments and believes it is essential that stringent controls be exercised over the receipt and identification of critical components.

76. Several comments noted that the reserve-sampling requirement in proposed § 820.81(a) is not necessary for some critical components.

The Commissioner agrees with the comments, but does not believe the regulation should be changed because § 820.81(a) does not impose a general reserve-sampling requirement. For certain critical components, such as the power source of a cardiac pacemaker, a manufacturer should maintain a reserve sample of the component because experience has shown that, in a small number of instances, the component may prematurely fail during its expected life. The maintenance of a reserve sample provides the manufacturer with a factual basis for determining the actual, as opposed to the expected, life of the critical component and allows for the identification of troublesome areas so that corrective action may be undertaken. In developing procedures to implement § 820.81(a) each manufacturer has some flexibility to determine the quantity needed for analysis and reserve, thus reducing the burden on manufacturers. If a manufacturer has good reasons to believe that it is not necessary to maintain a reserve sample of a critical component, then the manufacturer need not do so. However, the manufacturer should be prepared to explain these reasons to FDA.

77. Several comments on proposed § 820.81(a) suggested that the wording of the proposed requirement concerning identification of critical components could be interpreted to mean that each critical component must be identified with control numbers upon receipt.

The Commissioner points out that § 820.81(a) requires only that each lot of critical components be identified with a control number(s) upon receipt.

78. One comment said the requirement in proposed § 820.81(b) should not require that a component supplier agreement take the form of a separate document. Several comments noted that the component supplier agreement is often spelled out in the purchase order specifications.

The Commissioner notes that the proposed regulations did not specify that the written agreement must be contained in a separate document and agrees that such agreement could be contained in a purchase order. Therefore, he believes that no change in the regulation is necessary.

79. Many comments objected to the requirement of a component supplier agreement proposed in § 820.81(b) because it is not always possible to obtain such an agreement, particularly in the instance of component suppliers who furnish standand "off-the-shelf" components.

The Commissioner agrees with the comments and is revising the regulation to require such an agreement only where possible.

PRODUCTION AND PROCESS CONTROLS

80. One comment suggested that manufacturing specifications and process requirements in proposed § 820.100 should not apply to all manufacturing operations.

The Commissioner disagrees with the comment and notes that § 820.5 states that the quality assurance program shall be appropriate to the specific device manufactured. This flexible approach enables manufacturer to exercise judgment in determining which specifications and/or processing procedures for a particular device need to be established, implemented, and controlled. The Commissioner is revising the final rule for clarity.

81. One comment on proposed § 820.100(a)(1) said these controls should also apply to device labeling.

The Commissioner agrees but notes that subpart G of the final regulation requires adequate controls for labeling.

82. Several comments suggested modification of proposed § 820.100(a)(2), which would require that specification changes, including changes made concerning devices already distributed, shall be subject to controls as great as or greater than those applied to the original design before the changes. The comments suggested that this requirement apply only to specification changes affecting device safety or effectiveness.

The Commissioner rejects the suggestion because most specification changes could directly or indirectly affect device safety and effectiveness. This requirement is revised in the final regulation to clarify the intent. The requirement now states that specification changes shall be subject to controls as stringent as those applied to the original design specifications of the device. Such changes shall be approved and documented by a designated individual(s) and shall include the approval date and the date the change becomes effective.

83. Several comments suggested that the requirement in proposed § 820.100(a)(2) to document all specification changes and implementation dates for such changes is too broad and would be unnecessarily burdensome to the manufacturer.

The Commissioner disagrees with these comments because he believes it is important to document the relationship between the date a specification change is approved and the date a specification change is implemented. The Commissioner is aware of device recalls that were caused by the failure of manufacturers to document changes made in production specifica-

tions. The Commissioner is revising § 820.100(b)(1) to clarify the intent.

84. Several comments objected to proposed § 820.100(b)(2), which requires that there be a formal approval procedure for any change in the manufacturing process of a device. These comments objected to the requirement on the ground that it is unnecessary. Many comments recommended that approval of changes in the manufacturing process be limited to those changes affecting device safety, performance, or effectiveness because not all manufacturing process changes require formal approval.

The Commissioner rejects these comments because he believes that a formal approval procedure should be established for any change in the manufacturing process. The Commissioner notes that the requirement permits a manufacturer to develop a formal approval procedure that is appropriate to the device being manufactured. The nature of the manufacturing process and the potential impact of any change in the device should be considered in determining an appropriate and adequate formal approval procedure. The Commissioner is revising this requirement to clarify the intent.

85. Many comments suggested that the use of the term "statistical control" in proposed § 820.100(c), regarding ongoing trend analysis, is confusing and essentially duplicates the requirment in § 820.100(b).

The Commissioner agrees that § 820.100(c) duplicates § 820.100(b) and is deleting § 820.100(c) from the final regulation.

86. Several comments recommended changing the requirement in proposed § 820.101(a) to state that critical operations shall be performed by qualified individuals or suitable equipment and shall be suitably verified. The comment suggested that the word "qualified" is more appropriate than the word "designated."

The Commissioner rejects the comment because the intent of proposed § 820.101(a) is to assure that manufacturers assign responsibility for each critical operation. The Commissioner believes that although many individuals may be qualified to perform a critical operation, one or more individuals should be specifically "designated" to assure accountability for that operation.

87. Several comments suggested that the information required in proposed § 820.101(b), regarding a record of critical operations, is also required under proposed § 820.115, regarding reprocessing of devices and components.

The Commissioner rejects the comments. Section 820.115 *Reprocessing of devices or components* establishes general requirements for all finished devices. The requirements of § 820.101(b) regarding records of critical operations apply to critical devices only.

88. One comment objected to the requirement in proposed § 820.101(b) that the individual performing the critical operation record that operation in the device history record as required in § 820.185(a) for critical devices. It was noted that proposed § 820.185(a) permits the device history record to include or reference such operation documentation.

The Commissioner agrees with the comments, and § 820.185(a) is revised to state that any individual responsible for the performance of a critical operation shall record or reference that operation in the device history record.

89. One comment objected to the requirement in proposed § 820.101(c), that the device history record identify each critical component of the device. The comment suggested that it would be most difficult and burdensome to identify each critical component in the device history record.

The Commissioner notes that the requirement should not be interpreted to mean that each individual critical component must be individually identified in the device history record. He intended to provide that a component may be identified as part of a lot, and he is amending § 820.195(b)(1) in the final regulation to clarify that a critical component may be designated merely by a lot number. The Commissioner has also determined that the requirement in proposed § 820.101(c) is also required by proposed § 820.185(b)(1). Accordingly, the Commissioner is deleting § 820.101(c).

90. Many comments objected to the requirement in proposed § 820.115(a) that all rejected devices that are subsequently reprocessed be subject to another complete final inspection. The comments suggested that the reason for rejection should determine the nature of the reinspection; that a device reworked for a cosmetic defect, such as a scratched surface, does not require a complete final inspection; and that only the rejected part or area of the device needs to be reinspected.

The Commissioner agrees with the comments and is revising § 820.115(a) of the final regulation to state that reprocessing procedures shall be established, implemented, and controlled to assure that the reprocessed device or component meets the original, or subsequently modified and approved, specifications.

91. One comment recommended that the reinspection of a reprocessed device, as required in proposed § 820.115(b), not be required to assure compliance with all specifications, but only with that specification the deviation from which necessitated the reprocessing.

The Commissioner agrees, and § 820.115(b) is amended in the final regulation to require that any device rejected during finished device inspection and later reprocessed shall be subject to another complete final inspection for any characteristics of the device which may be adversely affected by such reprocessing.

92. One comment objected to the requirement in proposed § 820.116(a) that there shall be a formal approval procedure for instituting a new, or altering an approved, reprocessing procedure. The comment noted that the requirement implied that original specifications cannot be changed or updated without prior written approval.

The Commissioner disagrees with the comments. Section 820.116(a) of the final regulation permits changes in original specifications without prior written approval if a manufacturer has established a formal approval procedure for instituting a new, or altering an approved, reprocessing procedure that does not require prior written approval.

93. Two comments recommended that the requirement in proposed § 820.116(a) that reprocessing procedures be designed so that the reprocessed device or component meets the same or equal specifications as the original device or component be changed to make the requirement consistent with § 820.115(b).

The Commissioner agrees with the comments, and § 820.116(a) of the final regulation is revised to state that any critical device or component subject to reprocessing procedure shall conform to the original, or subsequently modified and approved, specifications.

In addition, the Commissioner has revised § 820.116(a) for clarity.

94. Several comments on proposed § 820.116(b) regarding reprocessing control suggested that all written testing and sampling procedures be documented to assure that any reprocessed critical device or component conform to original specifications. It was suggested that such written procedures not be specifically located in the quality control manual as required in proposed § 820.116(b).

The Commissioner agrees with the comments, and § 820.116(b) of the final regulation is revised to require that these procedures be contained or referenced in the device master record. The Commissioner is deleting proposed §820.190, which required the maintenance of a quality assurance manual, because all the information required to be included in the manual is already required to be included in the master device record. Hence, proposed § 820.190 is unnecessary.

95. Several comments on proposed § 820.116(b) noted that, in some instances, a manufacturer may not want a reprocessed device or component to meet original specifications.

The Commissioner agrees with the comments, and § 820.116(b) of the final regulation is revised to require that reprocessed devices and components meet the original, or subsequently modified and approved, specifications.

96. Several comments on proposed § 820.116(c), regarding failure investigation, suggested that failure investigations be undertaken whenever any device or any of its components fails to meet performance specifications, regardless of whether the failed device is critical or not. The comments noted that the failure of noncritical devices can have deleterious effects on the health of a patient.

The Commissioner agrees that the protection of the public requires that all such failures be investigated and documented, and the requirement is amended accordingly. The Commissioner has also determined that this requirement for failure investigation should apply to any device that fails after the device has been released for distribution and should be located in Subpart I—Device Evaluation. The Commissioner is adding new § 820.162 to make this change.

PACKAGING AND LABELING CONTROL

97. Many comments on proposed § 820.120(a), concerning label integrity, suggested that requiring labels to be attached to devices would be impractical for certain types of devices, such as ophthalmic lenses, pacemakers, bone screws, and dental products.

The Commissioner notes that labels may be attached to outside containers or packages and that it is not a mandatory requirement that the label be attached to the device itself. Additionally, the Commissioner is amending the final regulation to require that a designated individual(s) proofread samples of labeling for accuracy before the labels and other labeling are released to inventory. The Commissioner finds that this requirement is necessary to assure labeling integrity and control. This requirement will minimize the possibility of labeling mixups, a problem which has resulted in many device recalls.

98. Several comments suggested that proposed § 820.120(b), which requires spatial separation of the device labeling operation, is necessary only for materials that look alike. It was stated that it is not physically practical in many small companies to completely separate assembly, labeling, and packaging areas. The Commissioner does not intend and is not requiring that labeling operations be separated from packaging or assembly operations. However, the Commissioner believes that labeling operations for different devices should be separated from similar labeling operations in a manner designed to prevent mixups. Therefore, he is retaining the requirement.

99. Many comments on proposed § 820.120(b) argued that the requirement for the separation of packaging and labeling operations could be met by using methods or procedures other than physical or spatial separation.

The Commissioner rejects the comments. Physical or spatial separation of packaging or labeling operations for different devices is the most effective means of preventing mixups.

100. Several comments objected to proposed § 820.120(c) regarding area inspection and containing requirements for inspection of packaging and labeling areas. It was suggested that it would be burdensome for a manufacturer to require that the area be reinspected by a designated individual other than the operator to assure that device labeling materials from prior operations do not remain in the area.

The Commissioner agrees, and the final regulation is amended to delete the requirement that the designated individual not be the individual actually responsible for the labeling operation.

101. Many comments on proposed § 820.120(c) said that in manufacturing any device, especially a large piece of equipment, the possibility of mislabeling is remote and that recording area inspections in the device history record would only amount to excessive, useless recordkeeping.

The Commissioner agrees with the comments and is deleting the requirement that a record of such inspection be maintained because he believes that compliance with the requirements of § 820.120(d) of the final regulation will be sufficient to prevent that mixups in device labeling.

102. Several comments on proposed § 820.121 suggested that the labels and labeling materials for critical and noncritical devices alike should be stored and maintained in a manner to provide proper identification and to prevent mixups.

The Commissioner agrees that proper storage of labels and labeling for critical and noncritical devices is an important safeguard designed to prevent mixups. He is adding new § 820.120(d) to the final regulation to require that labels and labeling be stored and maintained in a manner that provides proper identification and is designed to prevent mixups.

103. Several comments on proposed § 820.121 suggested that labeling materials issued for both critical and noncritical devices should be examined for identity and, where applicable, expiration dates, control numbers, storage instructions, handling, and additional processing instructions.

The Commissioner agrees that labeling materials for critical and noncritical devices alike should be examined for identity to maintain labeling integrity and to provide necessary control. He is adding new § 820.120(e) to the final regulation to require that labeling materials issued for devices be examined for identity and, where applicable, expiration dates, control numbers, storage instructions, handling instructions, and additional processing instructions.

104. Several comments suggested that in the device master record, a record should be maintained to document that an individual has examined labeling materials for identity.

The Commissioner agrees that a record of such examination of labeling materials, which includes the date and person performing the examination, should be maintained. The Commissioner is adding new § 820.120(e) to the final regulation to make this change.

105. Several comments expressed concern that proposed § 820.121, which requires that all labeling materials be examined for the presence of expiration dates and storage instructions, is not appropriate for all critical devices.

The Commissioner agrees with the comments. The final regulation is revised by adding the phrase "where applicable" to § 820.120(e) so that the requirement of compliance with the provision depends upon the particular characteristics of the device.

106. Many comments objected to proposed § 820.121(a), which required that statistically selected samples of critical device labels and labeling be proofread for accuracy. It was suggested that statistical methods are not always the best methods. It was further suggested that samples of all labels and labeling, not just labeling pertaining to critical devices, should be proofread before being released to production.

The Commissioner accepts the comments, and the reference to a "statistically selected sample" is deleted. He is revising § 820.121(a) of the final regulation by applying the requirement to proofread samples of labeling to noncritical as well as critical devices because it also is important that the labeling of noncritical devices be accurate. In addition, the Commissioner is substituting the term "labels" for the term "labeling materials" in § 820.121(a) to clarify that the control number required for a critical device shall appear on the label of the critical device.

107. Several comments on proposed § 820.121(c) restricting personnel access to critical device labeling recom-

mended that the restriction apply only "where applicable."

The Commissioner disagrees with the comments because it is important that access to labels and labeling be limited to authorized personnel to prevent labeling mixups.

108. A few comments questioned the necessity of destroying or altering excess printed labels bearing control numbers as required in proposed § 820.121(d). The comments said this was costly and sometimes unnecessary.

The Commissioner agrees, and proposed § 820.121(d) is deleted from the final regulation.

109. One comment suggested that proposed § 820.130, regarding device packaging and providing that "Package design, construction, and material shall be adequate to protect the device during customary conditions of processing, storage, handling, and shipment," be changed by placing the word "shipping" before the term "package design." The comment suggested that the requirement should apply only to the shipping package.

The Commissioner rejects the comments and points out that § 820.130 on device packaging in the final regulation applies to all packaging, whether or not the immediate container or the shipping container, so as to assure protection of the device during storage and shipment.

110. Several comments recommended that proposed § 820.131(a), regarding critical device package design, and requiring that the device package be designed and constructed to protect the device from alteration or damage by expected external factors, exclude any reference to external energy factors since these factors were only one example of many factors for which provision must be made.

The Commissioner agrees with the comments, and proposed § 820.131(a) is deleted from the final regulation. The Commissioner finds that the requirements of § 820.130 in the final regulation are sufficient to communicate the intent of proposed § 820.131(a).

111. Several comments suggested deleting proposed § 820.131(b), regarding critical device storage and handling protection and requiring that the device containers and packages be designed to withstand any reasonably anticipated factors to be encountered under normal and common storage and handling conditions of the device until ready for its intended use, because proposed § 820.131(b) duplicated the requirements of § 820.130.

The Commissioner agrees with the comments, and proposed § 820.131(b) is deleted from the final regulation. The Commissioner believes that the requirements of § 820.130 are adequate to assure that device packaging is properly controlled and that additional requirements for critical devices are unnecessary.

Holding, Distribution, and Installation

112. Several comments objected to the wording in proposed § 820.150, which stated that there shall be written procedures for finished device warehouse control and distribution to assure that only those devices authorized for release are distributed. It was suggested that the term "devices authorized for release" be changed to "devices approved for release," as authorization presumes approval.

The Commissioner agrees with the comments, and the amendment is made. Section 820.150 is also revised to clarify that the oldest approved devices shall be distributed first where a device's quality or fitness for use deteriorates over time.

113. Many comments on proposed § 820.151 suggested that the dealer or distributor of a critical device be required to record the batch or lot number of that critical device upon sale to a user so that the device could be more readily located in the event of a recall.

The Commissioner is not adopting the comment. The Commissioner has decided that this regulation should not apply only to persons who only distribute devices, as is stated in § 820.1 *Scope*. Dealers or distributors may record batch or lot numbers if they believe, or they agree with, the manufacturer that a particular device requires such traceability. Future FDA regulations may address distributor recordkeeping requirements.

114. Several comments objected to proposed § 820.150, which required for critical devices the maintenance of distribution records that include the name and address of the consignee, the name and quantity of devices, the date shipped, and the control number used. The comments suggested that the recordkeeping requirement should be flexible enough to permit the manufacturer to make reference to the location of the required information.

The Commissioner agrees, and the final regulation is amended accordingly.

Device Evaluation

115. Many comments on proposed § 820.160, regarding finished device inspection, suggested deleting the requirement that a device be tested under those conditions in which it is to operate. Comments noted that such testing is part of the design verification process. They pointed out that design verification results in the development of testing programs to ensure that each lot of finished devices conforms to the design requirements; and, as long as each lot passes these tests satisfactorily, it is unnecessary to test the device repeatedly under normal operating conditions. Many comments suggested that it was impossible to test a device under those conditions in which it is to operate.

The Commissioner agrees with the comments, and § 820.160 is revised so that it no longer is an absolute requirement. Instead, it requires that, where practical, a device be selected from a production run and tested under simulated-use conditions and, where necessary, tested for conformance with device specifications. The Commissioner notes that § 820.181 *Device master record* requires the manufacturer to identify where it is necessary that a device be tested for conformance with its specifications. Any device which requires calibration or adjustment, to assure that it is in proper operating condition or otherwise fit for its intended use, should be tested carefully as part of the finished device inspection. The manufacturer should be prepared to explain to FDA the decisions made about the appropriateness and necessity of finished device testing.

116. One comment objected to the requirement in proposed § 820.160 that sampling plans for testing and release of the device be statistically validated.

The Commissioner accepts the comment, and § 820.160 is revised to require in the final regulation that sampling plans for checking and release of a device be based on an acceptable statistical rationale, without necessarily being statistically validated.

117. Many comments recommended deletion of the requirement in proposed § 820.161 for critical devices that a designated individual assure that all records and documentation required for the device history record are correct, because it was cumbersome and impractical and would result in unnecessary duplication of effort. Further, it was argued that the economic burden of performing double checks is not warranted because the device history record will already contain the signatures of responsible individuals, thus attesting to the correctness of the information in this record. It was suggested that the designated individual be required only to assure that the contents of the device history record are "consistent with the release criteria" for the device.

The Commissioner is responding to the comments by revising § 820.161 to require in the final regulation that a designated individual(s) be responsible for assuring that all records and documentation required for the device history record are present, complete, and consistent with the release criteria.

In addition, the Commissioner is revising § 820.161 to require that a critical device or component which does

not meet its performance specifications during finished device inspection shall be investigated and that a written record of the investigation, including conclusions and followup, shall be made. The Commissioner believes that this requirement, which was previously found in proposed § 820.116(c), is more properly located in § 820.161 *Critical devices, finished device inspection.*

RECORDS

118. Many comments on the general requirements in proposed § 820.180 for records and reports objected to the phrase "parts 820 through 829." Comments suggested that this phrase be deleted because, of the cited parts, only part 820 is now in existence.

The Commissioner accepts the comments, and the regulation is amended accordingly.

119. The Commissioner is revising § 820.180 to clarify the intent of the records requirements. The Commissioner is requiring that all records required by part 820 be maintained at the manufacturing establishment or other reasonably accessible location. He is also including in the regulation the requirement of section 704(e) of the act (21 U.S.C. 374(a)) that records required to be kept regarding devices shall be available for review and copying by FDA representatives. This change responds to a comment asking whether FDA would have access to inspect records required to be kept under part 820. The Commissioner notes that FDA will examine these records to determine whether manufacturers are complying with the recordkeeping and documentation requirements of the regulation and with the act.

The Commissioner also notes that the principal reason for stipulating that all records required by part 820 shall be maintained at the manufacturing establishment or other reasonably accessible location is for the benefit of the manufacturer. By maintaining these records at the manufacturing establishment or other reasonably accessible location, responsible officials of a manufacturer can exercise control and accountability over the entire manufacturing process and thereby maximize the probability that the finished device conforms to its design specifications. The requirement helps assure that responsible officials at the manufacturing establishment have ready access to those documents essential for conducting self-inspections, complaint investigations, failure analyses, and audits.

120. Several comments on proposed § 820.180(b) concerning record retention period recommended that a provision be made regarding the record retention period for devices which have very short lifetimes. Many of these comments also noted that there were devices with an indefinite life expectancy. It was suggested that the period required for record retention be left to the manufacturer.

The Commissioner concludes that the requirement on record retention period will remain unchanged. The minimum record retention period will continue to be 2 years, a time period consistent with the biennial inspection requirement in section 510(h) of the act (21 U.S.C. 360(h)) for class II and class III devices. In the event that the record retention imposes a hardship on the manufacturer, a variance from the requirement may be requested. It should be recognized that for devices with an indefinite life expectancy the regulation states that such records shall be maintained "for a period of time consistent with the design and expected life of the device."

121. Many comments suggested that proposed § 820.180(b) be amended to provide the manufacturer with the option of retaining photostatic or other reproductions of a record.

The Commissioner agrees and is amending this section. However, a manufacturer must take steps to assure that any reproductions are true and accurate copies of the original. Where written notes, erasure marks, or other changes are not apparent on the reproduction, a notation of this fact should be clearly indicated on the reproduction of the record, and the hard copy of the record should be retained for the required length of time.

122. Several comments expressed confusion about the requirements in proposed § 820.181 on what is to be maintained in the master device record and the requirements in proposed § 820.184 on what is to be maintained in the device history record.

The Commissioner believes that both sections already are clear, but has changed both sections to clarify further the intent of the requirements.

123. Many comments on proposed § 820.181, regarding the master device record, suggested rewording to provide that references can be made to locations within the manufacturing facility where various records are housed. Comments noted that duplicative records for every device would be costly and impractical.

The Commissioner agrees with the comments. Section 820.181 of the final regulation is amended to state that the device master record shall include, or refer to the location of, all specifications and procedures for the manufacture of each type of device.

124. Several comments on proposed § 820.181 objected to the phrase "each separate device entity" because this phrase was not clear and could encompass devices that differ only in size, shape, packaging, or color. It was suggested that the intent of this requirement be clarified.

The Commissioner agrees, and § 820.181 in the final regulation is revised to provide that the master device record shall include or reference all specifications and procedures for each type of device. It will be unnecessary to include in the device master record duplicate specifications for each separate device entity. However, the master device record shall include, or reference the location of, any unique specifications and procedures for the manufacture of devices which differ only in size, shape, packaging, or color.

125. Several comments on § 820.180 suggested that the general requirements regarding the master device record applicable to both noncritical and critical devices were more inclusive than the separate requirements applicable to critical devices. The comments pointed out that the sentence, "The master device record shall include all specifications and procedures or appropriate references for each separate device entity" was broader than the device master record requirements for critical devices. These comments noted that the critical device requirements in proposed § 820.182, in paragraph (a) regarding device specification, paragraph (b) regarding production process specifications, paragraph (c) regarding quality control specifications, and paragraph (g) regarding packaging specifications were merely types of specifications already required by proposed § 820.180.

The Commissioner agrees with the comments, and §§ 820.181 and 820.182 are revised in the final regulation to clarify the intent of the requirements and to preserve the distinction between noncritical and critical device requirements.

126. Several comments on proposed § 820.182, regarding the critical device master record, objected to the proposed requirement that all specifications and procedures on critical devices be included or referenced in a single record.

The Commissioner rejects the comments. It is essential that a single source document for each device manufactured be assembled, maintained, and consulted when necessary by the manufacturer. The Commissioner notes that specifications and procedures for critical devices may be referenced in the device master record as long as they are available for inspection at the manufacturing site or other reasonably accessible location.

127. Several comments on proposed § 820.182(f), regarding labels and labeling, recommended that copies of promotional material not be included in the device master record because such

material is not part of the manufacturing process.

The Commissioner agrees with the comments, and § 820.182(f) is deleted from the final regulation. Although promotional materials other than labeling will not be required as part of the device master record, these materials should be available to FDA representatives at the manufacturing establishment.

128. Many comments suggested that the intent of proposed § 820.184 be clarified. The comments expressed confusion over the requirement that sufficient records be maintained to demonstrate conformance to specifications, and sought guidance as to what was meant by "sufficient records."

The Commissioner agrees with the comments, and the final regulation is revised to require that a device history record be maintained to demonstrate that the device is manufactured in accordance with the device master record. The device history record shall include or refer to the location of the following information: The dates of manufacture, the quantity manufactured, the quantity released for distribution, and any control number used.

129. Several comments expressed confusion about proposed § 820.185 (b)(1), on control numbers used for component documentation. The comments said it would be unnecessarily burdensome and costly to require manufacturers to identify each critical component by a control number.

The Commissioner advises that he did not intend that each critical component carry a control number. The final regulation is changed to provide that critical components may be designated in the device history record by a control number identifying a particular lot of critical components. The Commissioner has also revised § 820.185 for clarity and consistency of language.

130. Many comments recommended that proposed §§ 820.190 and 820.191, regarding a quality control manual, be deleted because all the information required in the quality control manual is required in proposed § 820.181 *Master device record.*

The Commissioner agrees that maintenance of a quality control manual would duplicate requirements of the device master record, and proposed §§ 820.190 and 820.191 are deleted from the final regulation.

131. Several comments addressed proposed § 820.195, regarding checks of automated data processing concerning critical devices. The comments said the requirement should be limited to data processing information used for manufacturing or quality assurance purposes and argued that it is unnecessary to apply this requirement to data processing activities such as billing and personnel files. Several comments said the manufacturer should not be required to make and to store a duplicate copy of computerized information at a separate geographical location because hard copy reports can be generated and made available to FDA upon request.

The Commissioner agrees with these comments, and the final regulation is amended to apply only to automated data processing used for manufacturing or quality assurance purposes. The Commissioner also is deleting the requirement for maintenance of a duplicate copy of computerized information.

132. Many comments on proposed § 820.198(a), regarding complaint files, argued that any requirement to maintain a complaint file must be tempered by the fact that each firm will define a complaint somewhat differently. The comments suggested that there are a great many customer inquiries which do not relate to product safety or effectiveness and, therefore, are not complaints.

The Commissioner finds that the description of what is meant by the term "complaint" found in proposed § 820.198(a) is sufficient to communicate the kinds of complaints that must be reviewed and maintained. However, to correct an oversight in the proposal, he has specified that the requirement to maintain a complaint file applies to complaints relative to safety (as well as identity, quality, durability, reliability, effectiveness, or performance) of a device.

133. Several comments suggested that a manufacturer should have the flexibility to designate a unit other than the quality control unit to maintain, review, and investigate, where necessary, complaints made about devices.

The Commissioner agrees, and the final regulation is amended by substituting the term "formally designated unit" for "quality control unit."

134. Several comments objected to the requirement in proposed § 820.198(b) that complaints about injury, death, or safety be maintained separately from other complaints. They suggested that there is no useful purpose for separating files and that it should be the manufacturer's prerogative to file complaints in any manner he sees fit.

The Commissioner disagrees with the comments because complaints dealing with an injury deserve special attention when there is a possibility that the failure of a device is responsible for the injury. The Commissioner also believes that those complaints about a device's identity, quality, durability, reliability, safety, effectiveness, or performance are often indicative of poor manufacturing practices requiring correction. In evaluating the adequacy and appropriateness of a quality assurance program, the Commissioner is interested in learning how a manufacturer investigates and follows up on such complaints.

To help assure that this investigation and followup occur, the Commissioner is amending the final regulation to require that a written record of each investigation of a complaint be maintained and be readily available at the manufacturing site in a file designated for device complaints. The Commissioner believes that this requirement will facilitate the effective enforcement of the act by assuring that complaint investigation reports are accessible to responsible company officials and to FDA representatives who, in turn, can determine whether necessary corrective action has been accomplished.

The Commissioner advises that FDA representatives will routinely examine a manufacturer's complaint file to determine whether those complaints that require followup have been properly investigated.

The Commissioner also is revising § 820.198 to clarify the requirements of this section.

135. Several comments said FDA should not cite section 519 of the act (21 U.S.C. 360i), regarding records and reports on devices, as part of the authority for Part 820. It was argued that FDA had not met the specific requirements of section 519 of the act. One comment said that findings must be made as to how each recordkeeping and reporting requirement satisfies section 519 of the act and that FDA cannot incorporate recordkeeping requirements under section 519 of the act in a GMP regulation but must issue a separate recordkeepng regulation. The comment also asserted that FDA could require manfacturers to maintain GMP records, but could not inspect them. The concern was that if the GMP regulation was promulgated under authority of section 519 as well as section 520(f) of the act and other provisions, FDA would have specific authority to inspect, copy, and verify required records under section 704(e) of the act (21 U.S.C. 374(e)).

The Commissioner rejects the comments. There is no reason why he cannot rely on section 519 of the act in establishing GMP recordkeeping and reporting requirements. Indeed, the legislative history indicates that Congress expected FDA to do so (H. Rept. No. 94-853, 94th Cong., 2d sess., 23). It would be illogical for FDA to have authority to require GMP records to be kept but not to see them.

The GMP records and reports requirements are promulgated under sections 519, 520(f), and 701(a) of the act. Section 519 of the act requires a

manufacturer of a device to maintain such records, make such reports, and provide such information as the Commissioner may by regulation reasonably require to assure that such device is not adulterated or misbranded and to otherwise assure its safety and effectiveness. The GMP recordkeeping and reporting requirements clearly are reasonable requirements under this general authority and, in addition, are consistent with limits on this authority in section 519(a)(1) through (5) of the act, as explained below. Section 519 does not require the Commissioner to make any findings. (Compare, for example, section 514(g) (2) and (3) of the act (21 U.S.C. 360d(g) (2) and (3)).)

Section 519(a)(1) of the act prohibits recordkeeping requirements that are unduly burdensome to a device manufacturer, taking into account the cost of complying with the requirements and the need for protection of the public health and the implementation of the act. The Commissioner has considered each recordkeeping requirement in Part 820 and has concluded that none is unduly burdensome considering the costs and the benefits. The FDA survey of manufacturing practices in 300 device establishments showed that 80 percent of the establishments inspected were already complying with the major recordkeeping requirements of the proposed device GMP. Thus, the majority of device manufacturers would only have to make minor changes to their current practices to be in full compliance with the GMP recordkeeping requirements. The more demanding recordkeeping requirements only apply to manufacturers of critical devices. FDA has deleted a number of duplicative or burdensome proposed requirements in response to comments. Any manufacturer who believes that a requirement, as it applies to that manufacturer, is unduly burdensome may request an exemption or variance.

Section 519(a)(2) of the act provides that procedural regulations for device reporting requirements shall require each FDA request for a report or information under the regulations to state the reason or purpose for the request and identify to the fullest extent practicable the desired report or information. Section 519(a)(3) of the act applies a similar requirement to other FDA requests for submission of a report or information on devices. Except for the provision in § 820.20(b) for FDA to request certification concerning manufacturers' audits of quality assurance procedures, Part 820 does not create any procedures for FDA to request reports or information and, thus, is not subject to section 519(a)(2) of the act. FDA generally will rely on the inspection procedures in section 704(e) of the act (which are referenced in § 820.180) to gain access to, and copying of, required records. FDA does not believe that notices of inspection under section 704 of the act are subject at section 519(a)(3) of the act, which governs "submissions" of reports.

The procedure in § 820.20(b) for requests of certification concerning audit reports complies with section 519(a)(2) of the act.

The agency's access to patient identification in complaint files is consistent with section 519(a)(4) of the act; this access is needed to determine the safety and effectiveness of devices, to verify required records, and, in some cases, to protect the individual's medical welfare.

Finally, the regulations comply with section 519(a)(5) of the act because they do not require manufacturers of class I devices to maintain records on information not in their possession. All records required to be maintained concern the manufacturers' own establishments and procedures. Moreover, the records are needed to determine whether the devices are adulterated and misbranded. Congress expected FDA to require manufacturers of class I devices to keep records on quality control where necessary to protect the public health (H.R. Rep., supra, 24).

136. A comment asked whether FDA would have authority to inspect records required under Part 820.

The answer is yes. FDA already has authority in section 704(a) of the act (21 U.S.C. 374(a)) to inspect records concerning "restricted devices." FDA believes that this authority clearly extends to complaint files and other GMP records for restricted devices. It is FDA's position that the term "restricted device" include articles which are prescription devices under 21 CFR 801.109. However, some device manufacturers disagree with FDA and have challenged FDA's records inspection authority under section 704(a) of the act, in several pending lawsuits.

In three related cases, the U.S. District Court for the Northern District of New York, in a written opinion dated April 6, 1978, disagreed with FDA's determination that the term "restricted device" includes preenactment prescription devices. *Becton, Dickinson and Company* v. *Food and Drug Administration, et al.* (Civ. Action No. 77-CV-181); *United States* v. *Becton, Dickinson and Company* (Civ. Action No. 77-CV-337); *In the matter of establishment inspection of Bard-Parker Division of Becton, Dickinson and Company* (Misc. 112) (N.D. NY). These cases are under appeal to the U.S. Court of Appeals for the Second Circuit. A contrary result was reached by the U.S. District Court for the Central District of California in a decision reinstating an inspection warrant, which was quashed by another judge 4 weeks earlier, that authorizes FDA to inspect records relating to restricted devices (cardiac pacemakers). *In the Matter of the Establishment Inspection of American Technology, Inc.*, Civil Action No. CV-1727-LEW (C.D. CA, decided June 5, 1978). The issue is also pending in one other judicial district.

The GMP regulation, however, does not deal directly with the issues in these cases (the scope of section 704(a) authority and the meaning of "restricted devices"). After Part 820 becomes effective, FDA will have clear authority under section 704(e) of the act to inspect and copy required GMP records, including complaint files, for all devices, whether or not restricted devices, and regardless of the outcome of the pending cases. After the effective date, a person who refuses to allow FDA to inspect a required GMP record, or who causes such a refusal, will have committed an act that is prohibited under section 301 (e) and (f) of the Act (21 U.S.C. 331 (e) and (f)) and will be subject to regulatory action under section 302 or 303 (21 U.S.C. 332 or 333). In addition, under sections 501(h) and 502(t)(2) (21 U.S.C. 351(h), 352(t)(2)), devices are adulterated and misbranded if they are the subject of required GMP records to which FDA is refused access. Such devices are subject to seizure.

IMPLEMENTATION

137. Many comments expressed concern about FDA's plan for implementing the regulation and particularly the effective date. Comments said the regulation should become effective 180 days to 18 months after final publication in the FEDERAL REGISTER, rather than 90 days after final publication as FDA had proposed. Others cautioned that the agency should be flexible in implementing this regulation because of the need for industry to accomplish any necessary changes in their manufacturing practices with minimum confusion and cost. The comments also suggested that a flexible implementation schedule would provide FDA with an opportunity to train field personnel.

The Commissioner has carefully reviewed each comment on effective date and agrees that it is desirable for FDA to summarize and restate clearly FDA's implementation strategy for this regulation.

This regulation has been under development for a long time. The device industry has had an extraordinary involvement in its development. Since 1973 the agency has encouraged device manufacturers to examine their manufacturing practices in light of the draft and proposed device GMP regulations. For several years FDA has en-

gaged in constructive dialog with representatives of the device industry to foster a better understanding of the agency's overall approach to device GMP's. Simply stated, this approach recognizes the need to develop a regulation applicable to all device manufacturers. The regulation should not be so specific as to specify for every type of device manufacturer exactly what it must do and how its manufacturing practices must be accomplished; but, rather the regulation should set forth general requirements applicable to all manufacturers, with additional requirements for manufacturers of critical devices. These GMP requirements are designed to be flexible so that a device manufacturer can develop a detailed set of procedures, as required by §§ 820.5 and 820.20, which take into account a device's special manufacturing needs without compromising strict adherence to quality assurance requirements. FDA will look at these detailed procedures and how they measure up to the requirements of Part 820 to determine whether a manufacturer is complying with the regulation and is operating in accordance with its own quality assurance program.

The Commissioner recognizes that certain GMP requirements may be inappropriate when applied to certain device manufacturers. A manufacturer who believes that a GMP requirement is not appropriate or possible in the manufacture of that manufacturer's devices may petition for an exemption or variance under the procedures in § 820.1(d).

The Commissioner believes this regulation should be implemented as soon as possible to reduce the need for many device recalls and to upgrade existing quality assurance practices of the device industry. Based on FDA's experience, the Commissioner believes that many device recalls have resulted from obvious deficiencies in the manufacturing process and could have been prevented if the manufacturer had taken reasonable steps to follow a quality assurance program. However, the Commissioner recognizes that it may be difficult or costly for some manufacturers to comply with the regulation within 90 days after the publication of the final regulation and agrees that a later effective date should be provided. Accordingly, the Commissioner has concluded that manufacturers will be required to comply with the regulation 150 days after its publication.

The Commissioner recognizes the concerns many manufacturers have about how FDA will implement this regulation and how FDA will explain the requirements of the regulation to the affected industry. The Commissioner recognizes that the manufacturer, not FDA, is primarily responsible for producing high quality devices. FDA will encourage voluntary compliance. The decisions a manufacturer makes to tailor specific manufacturing needs to quality assurance requirements will be carefully evaluated by FDA. The industry should understand, however, that this regulation has the force of law, and that violation of its provisions are a basis for seizure, injunction, and for prosecution.

As an initial communication effort, that agency has conducted 12 2-day meetings across the country to inform manufacturers about the requirements of the regulation. These meetings were cosponsored by the American Society for Quality Control (ASQC) and FDA's Bureau of Medical Devices and were announced in the FEDERAL REGISTER of March 7, 1978 (43 FR 9320).

In addition to these meetings, the agency is conducting training programs for its field personnel to assure uniformity and consistency of application of this regulation. FDA field personnel will conduct GMP inspections according to compliance programs developed by the Bureau of Medical Devices. These programs will be available to the public upon request in accordance with 21 CFR part 20, FDA's public information regulations.

FDA has prepared and is making available to the public an analysis of GMP deficiencies and device recalls, enforcement actions, and complaints in recent years. This analysis shows how compliance with the requirements of the regulation might have prevented device defects, consumer injuries, and recalls and will aid manufacturers in complying with the regulation. For devices which have been tentatively recommended for classification into class I (general controls), the Commissioner recognizes that future FDA regulations or orders may provide for some device manufacturers to be exempt from certain provisions of the law, including the GMP regulation as it applies to certain class I devices. For this reason, FDA will not initiate any program to conduct routine inspections of manufacturers' devices which panels have recommended for class I until final classification regulations are published. But if it is necessary to investigate a device manufacturer because of complaints about a device failure or other defect, FDA will not hesitate to make an inspection to determine whether, among other things, the manufacturer is complying with device GMP's.

Where FDA investigators observe deviations from the GMP regulation, manufacturers will have the opportunity to discuss differences of opinion not only with the investigators but also with management in the FDA district offices and, if necessary, the Office of the Associate Director for Compliance in the Bureau of Medical Devices.

Background data and information on which the Commissioner relies in promulgating this regulation have been placed on file for public review in the office of the hearing clerk (HFA-305), Food and Drug Administration, room 4-65, 5600 Fishers Lane, Rockville, Md. 20857. A list of these documents follows:

REFERENCES

1. "Hospital Statistics," American Hospital Association Annual Survey, 1977.
2. "Current Manufacturing Practices in 300 Medical Device Establishments," prepared by Office of Compliance, Bureau of Medical Devices, FDA, 1977.
3. Transcripts of Four Public Meetings on GMP Regulations, San Francisco, Calif.; Dallas, Tex.; Chicago, Ill.; Washington, D.C., November 1975.
4. Transcript of Device GMP Advisory Committee Meeting on Device GMP Regulations, Washington, D.C., August 4, 1977.
5. Transcript of Public Hearing on Device GMP Regulation, Washington, D.C., August 5, 1977.
6. Transcript of Device GMP Advisory Committee Meeting on Device GMP Regulations, Washington, D.C., October 27-28, 1977.
7. "Inspection of Medical Device Manufacturers," Compliance Program 7324.19, Compliance Program Guidance Manual, FDA, October 22, 1976.
8. "Inspection of Diagnostic Product Manufacturers," Compliance Program 7324.18, Compliance Program Guidance Manual, FDA, March 10, 1977.
9. "Economic Impact Assessment of Final Rulemaking: Good Manufacturing Practice Regulation for Manufacture, Packing, Storage and Installation of Medical Devices," prepared by Food and Drug Administration, Department of Health, Education, and Welfare, Bureau of Medical Devices, June 1978.
10. "Inflation Impact Assessment Questionnaire," prepared by Office of Compliance, Bureau of Medical Devices, FDA.
11. "List of Critical Devices," prepared by Office of Compliance, Bureau of Medical Devices, FDA.
12. "Working Draft on Quality Systems Terminology," prepared by the Writing Committee for the revision of ASQC A3-1971, ANSI Z1.7-1971 (Draft 3, Rev. O, February 1, 1978).

In conjunction with the final regulation on good manufacturing practices, the Commissioner is promulgating a conforming amendment to 21 CFR 809.20(b) relating to compliance of in vitro diagnostic products with the drug GMP's found in 21 CFR parts 210, 211, 225, 226, and 229. This conforming amendment reflects the new definition of "device" which, as a result of the Medical Device Amendments of 1976 (Pub. L. 95-265), now includes in vitro diagnostic products. Because the amendment to part 809 makes no substantive changes and is promulgated only to conform with existing regulations, the Commissioner

finds that notice and public procedure are unnecessary.

All in vitro diagnostic products will be subject to 21 CFR part 820 relating to GMP's for medical devices, after the effective date of part 820.

The Food and Drug Administration has carefully considered the environmental effects of the regulation and, because the action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 501, 502, 518, 519, 520(f), and 701(a) as amended, 52 Stat. 1049-1051 as amended, 1055, 90 Stat. 562-569 (21 U.S.C. 351, 352, 360h, 360i, 360j(f), 371(a))) and under authority delegated to the Commissioner (21 CFR 5.1), chapter I of title 21 of the Code of Federal Regulations is amended as follows:

1. Part 809 is amended in § 809.20 by revising paragraph (b) to read as follows:

§ 809.20 General requirements for manufacturers and producers of in vitro diagnostic products.

* * * * *

(b) *Compliance with good manufacturing practices.* In vitro diagnostic products shall be manufactured in accordance with the good manufacturing practices requirements found in part 820 of this chapter.

2. New part 820 is added to read as follows:

Subpart A—General Provisions

Sec.
820.1 Scope.
820.3 Definitions.
820.5 Quality assurance program.

Subpart B—Organization and Personnel

820.20 Organization.
820.25 Personnel.

Subpart C—Buildings

820.40 Buildings.
820.46 Environmental control.
820.56 Cleaning and sanitation.

Subpart D—Equipment

820.60 Equipment.
820.61 Measurement equipment.

Subpart E—Control of Components

820.80 Components.
820.81 Critical devices, components.

Subpart F—Production and Process Controls

820.100 Manufacturing specifications and processes.
820.101 Critical devices, manufacturing specifications, and processes.
820.115 Reprocessing of devices or components.
820.116 Critical devices, reprocessing of devices or components.

Subpart G—Packaging and Labeling Control

820.120 Device labeling.
820.121 Critical devices, device labeling.
820.130 Device packaging.

Subpart H—Holding, Distribution, and Installation

820.150 Distribution.
820.151 Critical devices, distribution, records.
820.152 Installation.

Subpart I—Device Evaluation

820.160 Finished device inspection.
820.161 Critical devices, finished device inspection.
820.162 Failure investigation.

Subpart J—Records

820.180 General requirements.
820.181 Device master record.
820.182 Critical devices, device master record.
820.184 Device history record.
820.185 Critical devices, device history record.
820.195 Critical devices, automated data processing.
820.198 Complaint files.

AUTHORITY: Secs. 501, 502, 518, 519, 520(f), 701(a), 52 Stat. 1049-1051 as amended, 1055, 90 Stat. 562-569 (21 U.S.C. 351, 352, 360h, 360i, 360j(f), 371(a)).

Subpart A—General Provisions

§ 820.1 Scope.

The regulation set forth in this part describes current good manufacturing practices for methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of all finished devices intended for human use. The regulation is intended to assure that such devices will be safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act. Part 820 establishes basic requirements applicable to finished devices, including additional requirements for critical devices. This regulation is not intended to apply to manufacturers of components or parts of finished devices, but such manufacturers are encouraged to use appropriate provisions of this regulation as guidelines. Manufacturers of human blood and blood components are not subject to this part, but are subject to part 606 of this chapter.

(a) *Authority.* This part 820 is established and promulgated under authority of sections 501, 502, 518, 519, 520(f), and 701(a) of the act (21 U.S.C. 351, 352, 360h, 360i, 360j(f), and 371(a)). The failure to comply with any applicable provisions in part 820 in the manufacture, packing, storage, or installation of a device renders the device adulterated under section 501(h) of the act. Such a device, as well as the person responsible for the failure to comply, is subject to regulatory action.

(b) *Limitations.* The current good manufacturing practice regulation in part 820 supplements regulations in other parts of this chapter except where explicitly stated otherwise. In the event it is impossible to comply with applicable regulations both in this part and in other parts of this chapter, the regulations specifically applicable to the device in question shall supersede any other regulations.

(c) *Applicability.* The provisions of part 820 shall be applicable to any finished device, as defined in this part, intended for human use, that is manufactured, imported, or offered for import in any State or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.

(d) *Exemptions or variances.* Any person who wishes to petition for an exemption or variance from any device good manufacturing practice requirement is subject to the requirements of section 520(f)(2) of the act. Petitions for an exemption or variance shall be submitted according to the procedures set forth in § 10.30 of this chapter, the Food and Drug Administration's administrative procedures.

§ 820.3 Definitions.

(a) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321-392)).

(b) "Audit" means a documented activity performed in accordance with written procedures on a periodic basis to verify, by examination and evaluation of objective evidence, compliance with those elements of the quality assurance program under review. "Audit" does not include surveillance or inspection activities performed for the purpose of conducting a quality assurance program or undertaking complaint investigations or failure analyses of a device.

(c) "Component" means any material, substance, piece, part, or assembly used during device manufacture which is intended to be included in the finished device.

(d) "Control number" means any distinctive combination of letters or numbers, or both, from which the complete history of the manufacture, control, packaging, and distribution of a production run, lot, or batch of finished devices can be determined.

(e) "Critical component" means any component of a critical device whose failure to perform can be reasonably expected to cause the failure of a critical device or to affect its safety or effectiveness.

(f) "Critical device" means a device that is intended for surgical implant into the body or to support or sustain

life and whose failure to perform when properly used in accordance with instructions for use provided in the labeling can be reasonably expected to result in a significant injury to the user. Critical devices will be identified by the Commissioner after consultation with the Device Good Manufacturing Practice Advisory Committee authorized under section 520(f) of the act, and an illustrative list of critical devices will be available from the Bureau of Medical Devices, Food and Drug Administration.

(g) "Critical operation" means any operation in the manufacture of a critical device which, if improperly performed, can be reasonably expected to cause the failure of a critical device or to affect its safety or effectiveness.

(h) "Device history record" means a compilation of records containing the complete production history of a finished device.

(i) "Device master record" means a compilation of records containing the design, formulation, specifications, complete manufacturing procedures, quality assurance requirements, and labeling of a finished device.

(j) "Finished device" means a device, or any accessory to a device, which is suitable for use, whether or not packaged or labeled for commercial distribution.

(k) "Manufacturer" means any person, including any repacker and/or relabeler, who manufactures, fabricates, assembles, or processes a finished device. The term does not include any person who only distributes a finished device.

(l) "Manufacturing material" means any material such as a cleaning agent, mold-release agent, lubricating oil, or other substance used to facilitate a manufacturing process and which is not intended by the manufacturer to be included in the finished device.

(m) "Noncritical device" means any finished device other than a critical device.

(n) "Quality assurance" means all activities necessary to assure and verify confidence in the quality of the process used to manufacture a finished device.

§ 820.5 Quality assurance program.

Every finshed device manufacturer shall prepare and implement a quality assurance program that is appropriate to the specific device manufactured and meets the requirements of this part.

Subpart B—Organization and Personnel

§ 820.20 Organization.

Each manufacturer shall have in place an adequate organizational structure and sufficient personnel to assure that the devices the manufacturer produces are manufactured in accordance with the requirements of this regulation. Each manufacturer shall prepare and implement quality assurance procedures adequate to assure that a formally established and documented quality assurance program is performed. Where possible, a designated individual(s) not having direct responsibility for the performance of a manufacturing operation shall be responsible for the quality assurance program.

(a) *Quality assurance program requirements.* The quality assurance program shall consist of procedures adequate to assure that the following functions are performed: (1) Review of production records; (2) approval or rejection of all components, manufacturing materials, in-process materials, packaging materials, labeling, and finished devices; approval or rejection of devices manufactured, processed, packaged, or held under contract by another company; (3) identifying, recommending, or providing solutions for quality assurance problems and verifying the implementation of such solutions; and (4) assuring that all quality assurance checks are appropriate and adequate for their purpose and are performed correctly.

(b) *Audit procedures.* Planned and periodic audits of the quality assurance program shall be implemented to verify compliance with the quality assurance program. The audits shall be performed in accordanee with written procedures by appropriately trained individuals not having direct responsibilities for the matters being audited. Audit results shall be documented in written audit reports, which shall be reviewed by management having responsibility for the matters audited. Followup corrective action, including reaudit of deficient matters, shall be taken when indicated. An employee of the Food and Drug Administration, designated by the Food and Drug Administration, shall have access to the written procedures established for the audit. Upon request of such an employee, a responsible official of the manufacturer shall certify in writing that the audits of the quality assurance program required under this paragraph have been performed and documented and that any required corrective action has been taken.

§ 820.25 Personnel.

Each manufacturer shall have sufficient personnel with the necessary education, background, training, and experience to assure that all operations are correctly performed.

(a) *Personnel training.* All personnel shall have the necessary training to perform their assigned responsibilities adequately. Where training programs are necessary to assure that personnel have a thorough understanding of their jobs, such programs shall be conducted and documented. All employees shall be made aware of device defects which may occur from the improper performance of their specific jobs. Quality assurance personnel shall be made aware of defects and errors likely to be encountered as part of their quality assurance functions.

(b) *Personnel health and cleanliness.* Personnel in contact with a device or its environment shall be clean, healthy, and suitably attired where lack of cleanliness, good health, or suitable attire could adversely affect the device. Any personnel who, by medical examination or supervisory observation, appear to have a condition which could adversely affect the device shall be excluded from affected operations until the condition is corrected. Personnel shall be instructed to report such conditions to their supervisors.

Subpart C—Buildings

§ 820.40 Buildings.

Buildings in which manufacturing, assembling, packaging, packing, holding, testing, or labeling operations are conducted shall be of suitable design and contain sufficient space to facilitate adequate cleaning, maintenance, and other necessary operations. The facilities shall provide adequate space designed to prevent mixups and to assure orderly handling of the following: Incoming components; rejected or obsolete components; in-process components; finished devices; labeling; devices that have been reprocessed, reworked, or repaired; equipment; molds, patterns, tools, records, drawings, blueprints; testing and laboratory operations; and quarantined products.

§ 820.46 Environmental control.

Where environmental conditions at the manufacturing site could have an adverse effect on a device's fitness for use, these environmental conditions shall be controlled to prevent contamination of the device and to provide proper conditions for each of the operations performed pursuant to § 820.40. Conditions to be considered for control are lighting, ventilation, temperature, humidity, air pressure, filtration, airborne contamination, and other contamination. Any environmental control system shall be periodically inspected to verify that the system is properly functioning. Such inspections shall be documented.

§ 820.56 Cleaning and sanitation.

There shall be adequate written cleaning procedures and schedules to meet manufacturing process specifica-

tions. Such procedures shall be provided to appropriate personnel.

(a) *Personnel sanitation.* Washing and toilet facilities shall be clean and adequate. Where special clothing requirements are necessary to assure that a device is fit for its intended use, clean dressing rooms shall be provided for personnel.

(b) *Contamination control.* There shall be procedures designed to prevent contamination of equipment, components, or finished devices by rodenticides, insecticides, fungicides, fumigants, hazardous substances, and other cleaning and sanitizing substances. Such procedures shall be documented.

(c) *Personnel practices.* Where eating, drinking, and smoking by personnel could have an adverse effect on a device's fitness for use, such practices shall be limited to designated areas selected so as to avoid such an adverse effect.

(d) *Sewage and refuse disposal.* Sewage, trash, by-products, chemical effluents, and other refuse shall be disposed of in a timely, safe, and sanitary manner.

Subpart D—Equipment

§ 820.60 Equipment.

Equipment used in the manufacturing process shall be appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, and cleaning.

(a) *Maintenance schedule.* Where maintenance of equipment is necessary to assure that manufacturing specifications are met, a written schedule for the maintenance, adjustment, and cleaning of equipment shall be developed and adhered to. Such schedule shall be visibly posted on or near each piece of equipment, or be readily available to personnel performing maintenance activities. A written record shall be maintained documenting when scheduled maintenance activities are performed.

(b) *Inspection.* Periodic documented inspections shall be made to assure adherence to applicable equipment maintenance schedules.

(c) *Adjustment.* Any inherent limitations or allowable tolerances shall be visibly posted on or near equipment requiring periodic adjustments, or be readily available to personnel performing these adjustments.

(d) *Manufacturing material.* Manufacturing material, including a cleaning agent, mold-release agent, lubricating oil, or other substance used on or in the manufacturing equipment or the device, shall be subsequently removed from the device or limited to a specified amount that does not adversely affect the device's fitness for use. There shall be written procedures for the use and removal of such manufacturing material. The removal of such manufacturing material shall be documented.

§ 820.61 Measurement equipment.

All production and quality assurance measurement equipment, such as mechanical, automated, or electronic equipment, shall be suitable for its intended purposes and shall be capable of producing valid results. Such equipment shall be routinely calibrated, inspected, and checked according to written procedures. Records documenting these activities shall be maintained. When computers are used as part of an automated production or quality assurance system, the computer software programs shall be validated by adequate and documented testing. All program changes shall be made by a designated individual(s) through a formal approval procedure.

(a) *Calibration.* Calibration procedures shall include specific directions and limits for accuracy and precision. There shall be provisions for remedial action when accuracy and precision limits are not met. Calibration shall be performed by personnel having the necessary education, training, background, and experience.

(b) *Calibration standards.* Where practical, the calibration standards used for production and quality assurance measurement equipment shall be traceable to the national standards of the National Bureau of Standards, Department of Commerce. If national standards are not practical for the parameter being measured, an independent reproducible standard shall be used. If no applicable standard exists, an in-house standard shall be developed and used.

(c) *Calibration records.* The calibration date, the calibrator, and the next calibration date shall be recorded and displayed, or records containing such information shall be readily available for each piece of equipment requiring calibration. A designated individual(s) shall maintain a record of calibration dates and of the individual performing each calibration.

Subpart E—Control of Components

§ 820.80 Components.

Components used in manufacturing shall be received, stored, and handled in a manner designed to prevent damage, mixup, contamination, and other adverse effects. Components shall be quarantined prior to acceptance or clearly identified as not yet accepted.

(a) *Acceptance of components.* There shall be a written procedure for acceptance of components. A designated individual(s) shall accept or reject components. A record shall be maintained of component acceptance and rejection. Upon receipt, each shipping container of components shall be visually examined for damage. Where deviations from component specifications could result in the device being unfit for its intended use, components shall be inspected, sampled, and tested for conformance to specifications.

(b) *Storage and handling of components.* If the quality or fitness for use of components deteriorates over time, the components shall be stored in a manner to facilitate proper stock rotation. Component control numbers or other identifications shall be easily viewable. All obsolete, rejected, or deteriorated components shall be clearly identified and segregated from accepted components. Records shall be maintained of the disposition of all obsolete, rejected, or deteriorated components.

§ 820.81 Critical devices, components.

In addition to the requirements of § 820.80, the following requirements apply to critical devices:

(a) *Acceptance of critical components.* There shall be written procedures for the accepting, sampling, testing, and inspecting of all lots of critical components to assure that critical components conform to specifications. The number of units sampled from each lot of critical components shall be based upon an acceptable statistical rationale, the past quality history of the supplier, and the quantity needed for analysis and reserve. Each lot of critical components shall be identified with a control number(s) upon receipt. The percentage of defective critical components for each lot and the percentage of lots rejected shall be recorded and identified by supplier name.

(b) *Critical component supplier agreement.* Where possible, the manufacturer shall secure from the critical component supplier a written agreement whereby the supplier agrees to notify the manufacturer of any proposed change in a critical component. Where such an agreement exists, the manufacturer shall not accept such a change until the manufacturer has determined the impact of the change on the finished device.

Subpart F—Production and Process Controls

§ 820.100 Manufacturing specifications and processes.

Written manufacturing specifications and processing procedures shall be established, implemented, and controlled to assure that the device conforms to its original design or any approved changes in that design.

(a) *Specification controls.* (1) Procedures for specification control meas-

ures shall be established to assure that the design basis for the device, components, and packaging is correctly translated into approved specifications.

(2) Specification changes shall be subject to controls as stringent as those applied to the original design specifications of the device. Such changes shall be approved and documented by a designated individual(s) and shall include the approval date and the date the change becomes effective.

(b) *Processing controls.* (1) Where deviations from device specifications could occur as a result of the manufacturing process itself, there shall be written procedures describing any processing controls necessary to assure conformance to specifications.

(2) All processing control operations shall be conducted in a manner designed to assure that the device conforms to applicable specifications.

(3) There shall be a formal approval procedure for any change in the manufacturing process of a device. Any approved change shall be communicated to appropriate personnel in a timely manner.

§ 820.101 Critical devices, manufacturing specifications, and processes.

In addition to the requirements of § 820.100, the following requirements apply to critical devices:

(a) *Critical operation performance.* Any critical operation shall be performed by a suitable designated individual(s) or suitable equipment and shall be verified.

(b) *Record of critical operation.* Any individual responsible for the performance of a critical operation shall record or reference that operation in the device history record as required in § 820.185.

§ 820.115 Reprocessing of devices or components.

(a) Reprocessing procedures shall be established, implemented, and controlled to assure that the reprocessed device or component meets the original, or subsequently modified and approved, specifications.

(b) Any device rejected during finished device inspection and later reprocessed shall be subject to another complete final inspection for any characteristic of the device which may be adversely affected by such reprocessing.

§ 820.116 Critical devices, reprocessing of devices or components.

In addition to the requirements of § 820.115, the following requirements apply to critical devices:

(a) *Reprocessing procedures.* There shall be written procedures for any reprocessing associated with the production of a critical device or component. These procedures shall prescribe the equipment to be used in reprocessing and shall include any special quality assurance methods or tests. The procedures shall be designed so that the reprocessed device or component meets the original, or subsequently modified and approved, specifications. The procedures shall be designed to prevent adulteration, e.g., because of material, structural, or molecular change in the device or component due to reprocessing. Special care shall be taken to assure that the device or component to be reprocessed is clearly identified and separated from like devices or components not to be reprocessed. When there is constant reprocessing of a device or component, a determination of the effect of the reprocessing upon the device or component shall be made and documented. There shall be a formal approval procedure for instituting a new, or altering an approved, reprocessing procedure.

(b) *Reprocessing control.* Any critical device or component subject to reprocessing procedures shall conform to the original, or subsequently modified and approved, specifications. Written testing and sampling procedures to assure such comformity shall be contained or referenced in the device master record. Any prior quality assurance check shall be repeated on the reprocessed device or component if the reprocessing could adversely affect any performance characteristic previously inspected.

Subpart G—Packaging and Labeling Control

§ 820.120 Device labeling.

There shall be adequate controls to maintain labeling integrity and to prevent labeling mixups.

(a) *Label integrity.* Labels shall be designed, printed, and applied so as to remain legible during the customary conditions of processing, storage, handling, distribution, and use. Labels and other labeling shall not be released to inventory until a designated individual has proofread samples of the labeling for accuracy.

(b) *Separation of operations.* Each labeling or packaging operation shall be separated physically or spatially in a manner designed to prevent mixups.

(c) *Area inspection.* Prior to the implementation of any labeling or packaging operation, there shall be an inspection of the area where the operation is to occur by a designated individual to assure that devices and labeling materials from prior operations do not remain in the labeling or packaging area. Any such items found shall be destroyed, disposed of, or returned to storage prior to the onset of a new or different labeling or packaging operation.

(d) *Storage.* Labels and labeling shall be stored and maintained in a manner that provides proper identification and is designed to prevent mixups.

(e) *Labeling materials.* Labeling materials issued for devices shall be examined for identity and, where applicable, the correct expiration date, control number, storage instructions, handling instructions, and additional processing instructions. A record of such examination, including the date and person performing the examination, shall be maintained in the device history record.

§ 820.121 Critical devices, device labeling.

In addition to the requirements of § 820.120, the following requirements apply to critical devices:

(a) *Control number.* Labels issued for critical devices shall contain a control number.

(b) *Labeling check.* The signature of the individual who proofreads the labels and other labeling, and the date of the proofreading, shall be recorded.

(c) *Access restriction.* Access to the labels and other labeling shall be restricted to authorized personnel.

§ 820.130 Device packaging.

The device package and any shipping container for a device shall be designed and constructed to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution.

Subpart H—Holding, Distribution, and Installation

§ 820.150 Distribution.

There shall be written procedures for warehouse control and distribution of finished devices to assure that only those devices approved for release are distributed. Where a device's fitness for use or quality deteriorates over time, there shall be a system to assure that the oldest approved devices are distributed first.

§ 820.151 Critical devices, distribution records.

In addition to the requirements of § 820.150, adequate distribution records for critical devices shall include, or make reference to the location of: the name and address of the consignee, the name and quantity of devices, the date shipped, and the control number used. These records shall be retained as required by § 820.180(b).

§ 820.152 Installation.

Where a device is installed by the manufacturer or its authorized representative, the manufacturer or representative shall inspect the device after

installation to assure that the device will perform as intended. Where a device is installed by a person other than the manufacturer or its authorized representative, the manufacturer shall provide adequate instructions and procedures for proper installation.

Subpart I—Device Evaluation

§ 820.160 Finished device inspection.

There shall be written procedures for finished device inspection to assure that device specifications are met. Prior to release for distribution, each production run, lot or batch shall be checked and, where necessary, tested for conformance with device specifications. Where practical, a device shall be selected from a production run, lot or batch and tested under simulated use conditions. Sampling plans for checking, testing, and release of a device shall be based on an acceptable statistical rationale. Finished devices shall be held in quarantine or otherwise adequately controlled until released.

§ 820.161 Critical devices, finished device inspection.

In addition to the requirements of § 820.160, the following requirement applies to critical devices: A critical device or component which does not meet its performance specifications shall be investigated. A written record of the investigation, including conclusions and followup, shall be made. A critical device shall not leave the control of the manufacturer for distribution until all acceptance records and test results have been checked by a designated individual(s). Such individual(s) shall assure that all records and documentation required for the device history record are present and complete, and show that release of the device was consistent with the release criteria. Such individual(s) shall authorize, by signature, the release of the device for distribution.

§ 820.162 Failure investigation.

After a device has been released for distribution, any failure of that device or any of its components to meet performance specifications shall be investigated. A written record of the investigation, including conclusions and followup, shall be made.

Subpart J—Records

§ 820.180 General requirements.

All records required by this part shall be maintained at the manufacturing establishment or other location that is reasonably accessible to responsible officials of the manufacturer and to employees of the Food and Drug Administration designated to perform inspections. Such records shall be available for review and copying by such employees. Except as specifically provided elsewhere, the following general provisions shall apply to all records required by this part.

(a) *Confidentiality.* Those records deemed confidential by the manufacturer may be marked to aid the Food and Drug Administration in determining whether information may be disclosed under the public information regulation in Part 20 of this chapter.

(b) *Record retention period.* All required records pertaining to a device shall be retained for a period of time equivalent to the design and expected life of the device, but in no case less than 2 years from the date of release for commercial distribution by the manufacturer. Photostatic or other reproductions of records required by this part may be used.

§ 820.181 Device master record.

The device master record shall be prepared, dated, and signed by a designated individual(s). Any changes in the device master record shall be authorized in writing by the signature of a designated individual(s). Any approval forms shall be part of the device master record. The device master record for each type of device shall include, or refer to the location of, the following information:

(a) Device specifications including appropriate drawings, composition, formulation, and component specifications.

(b) Production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications.

(c) Quality assurance procedures and specifications including quality assurance checks used and the quality assurance apparatus used.

(d) Packaging and labeling specifications including methods and processes used.

§ 820.182 Critical devices, device master record.

In addition to the requirements of § 820.181, the device master record for a critical device shall include or refer to the location of the following information:

(a) *Critical components and critical component suppliers.* Full information concerning critical components and critical component suppliers, including the complete specifications of all critical components, the sources where they may be obtained, and written copies of any agreements made with suppliers under § 820.81(b).

(b) *Labels and labeling.* Complete labling procedures for the individual device and copies of all approved labels and other labeling.

§ 820.184 Device history record.

A device history record shall be maintained to demonstrate that the device is manufactured in accordance with the device master record. The device history record shall include, or refer to the location of, the following information: The dates of manufacture, the quantity manufactured, the quantity released for distribution, and any control number used.

§ 820.185 Critical devices, device history record.

In addition to the requirements of § 820.184, the following requirements apply to critical devices: There shall be a critical device history record for each control number, which shall include complete information relating to the production unit. This record shall identify the specific label, labeling, and control number used for each production unit and shall be readily accessible and maintained by a designated individual(s). The device history record shall include, or refer to the location of, the following:

(a) *Component documentation.* The documentation of each critical component used in the manufacture of a device shall include:

(1) *Control number.* The control number designating each critical component or lot of critical components used in the manufacture of a device.

(2) *Acceptance record.* The acceptance record of the critical component, including acceptance date and signature of the recipient.

(b) *Record of critical operation.* The record of, or reference to, each critical operation, identifying the date performed, the designated individual(s) performing the operation and, when appropriate, the major equipment used.

(c) *Inspection checks.* The inspection checks performed, the methods and equipment used, results, the date, and signature of the inspecting individual.

§ 820.195 Critical devices, automated data processing.

When automated data processing is used for manufacturing or quality assurance purposes, adequate checks shall be designed and implemented to prevent inaccurate data output, input, and programing errors.

§ 820.198 Complaint files.

(a) Written and oral complaints relative to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device shall be reviewed, evaluated, and maintained by a formally designated unit. This unit shall determine whether or not an investigation is necessary. When no investigation is made, the unit shall maintain a record that includes the reason and

the name of the individual responsible for the decision not to investigate.

(b) Any complaint involving the possible failure of a device to meet any of its performance specifications shall be reviewed, evaluated, and investigated. Any complaint pertaining to injury, death, or any hazard to safety shall be immediately reviewed, evaluated, and investigated by a designated individual(s) and shall be maintained in a separate portion of the complaint file.

(c) When an investigation is made, a written record of each investigation shall be maintained by the formally designated unit identified in paragraph (a) of this section. The record of investigation shall include the name of the device, any control number used, name of complainant, nature of complaint, and reply to complainant.

(d) Where the formally designated unit is located at a site separate from the actual manufacturing establishment, a duplicate copy of the record of investigation of any complaint shall be transmitted to and maintained at the actual manufacturing establishment in a file designated for device complaints.

Effective date. This regulation becomes effective December 18, 1978.

(Secs. 501, 502, 518, 519, 520(f), and 701(a) as amended, 52 Stat. 1049-1051 as amended, 1055, 90 Stat. 562-569 (21 U.S.C. 351, 352, 360h, 360i, 360j(f), 371(a)).)

Dated: July 13, 1978.

DONALD KENNEDY,
Commissioner of Food and Drugs.

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